JAN 17 1948

MEDICAL LIBRARY

VOLUME 74 NUMBER 5

AMERICAN JOURNAL

OF

DISEASES OF CHILDREN

EDITORIAL BOARD

CLIFFORD G. GRULEE, Chief Editor
Box 871, Evanston, Ill.

OSCAR M. SCHLOSS, New York
FRITZ B. TALBOT, Boston
A. A. WEECH, Cincinnati
H. F. HELMHOLZ, Rochester, Minn.
FRANCIS SCOTT SMYTH, San Francisco
JAMES L. WILSON, Ann Arbor, Mich.

NOVEMBER 1947

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second Class Matter Jan. 4, 1911, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

COPYRIGHT, 1948, BY THE AMERICAN MEDICAL ASSOCIATION

CONTENTS OF PREVIOUS NUMBER

OCTOBER 1947. NUMBER 4

Infarction of the Lung in Children. Ella Zuschlag, M.D., Rochester, Minn.

Vitamin C in the Blood and Urine of the Newborn and in the Cord and Maternal Blood. Brenton M. Hamil, M.D.; Bertha Munks, B.S.; Elsie Z. Moyer, M.S.; Mildred Kaucher, M.S., and Harold H. Williams, Ph.D., Detroit.

Thiamine, Riboflavin, Nicotinic Acid, Pantothenic Acid and Biotin in the Urine of Newborn Infants. Brenton M. Hamil, M.D.; Margaret Coryell, Ph.D.; Charlotte Roderuck, M.S.; Mildred Kaucher, M.S.; Elsie Z. Moyer, M.S.; Mary Ellen Harris, B.S., and Harold H. Williams, Ph.D., Detroit.

Penicillin in Treatment of Empyema in Children. George E. Prince, M.D., Gastonia, N. C., and William J. Temple, M.D., Louisville, Ky.

Fallacies Inherent in the Proband Method of Analysis of Human Pedigrees for Inheritance of Recessive Traits: Two Methods of Correction of the Formula. Madge T. Macklin, M.D., and Henry B. Mann, Ph.D., Columbus, Ohio.

Case Reports:

Streptomycin Treatment of Empyema Caused by Hemophilus Influenzae. A. J. Fisher, M.D., and E. B. Shaw, M.D., San Francisco.

Transposition of Aorta and Pulmonary Artery, with Intact Interventricular Septum, Patent Foramen Ovale and Closed Ductus Arteriosus. Béla Halpert, M.D., and Vernon D. Cushing, M.D., Oklahoma City.

Pneumococcic Meningitis: Recovery of an Infant Twenty-Five Days of Age Treated with Sulfadiazine and Penicillin. Sidney O. Cohlan, M.D., New York, and Nathaniel H. Solomon, M.D., Forest Hills, N. Y.

Progress in Pediatrics (Panel on Adolescence):

Nutritional Requirement of the Adolescent and Its Relation to the Development of Disease. J. A. Johnston, M.D., Detroit.

Physical Growth During Adolescence. Harold C. Stuart, M.D., Boston.

Improvement of Body Mechanics in Adolescent Children. Clifford D. Sweet, M.D., Oakland, Calif.

Endocrine Aspects of Adolescence. J. P. Pratt, M.D., Detroit.

Discussion.

Obituaries:

Hugh Kling Berkley, M.D.

Correspondence:

Convulsions Due to Use of Pertussis Vaccine. John A. Toomey, M.D., Cleveland.

News and Comment.

Abstracts from Current Literature.

Society Transactions:

Chicago Pediatric Society.

Book Reviews.

American Journal of Diseases of Children

VOLUME 74 NOVEMBER 1947 NUMBER 5

COPYRIGHT, 1948, BY THE AMERICAN MEDICAL ASSOCIATION

PRENATAL BOWING AND THICKENING OF TUBULAR BONES, WITH MULTIPLE CUTANEOUS DIMPLES IN ARMS AND LEGS

A Congenital Syndrome of Mechanical Origin

JOHN CAFFEY, M.D.
NEW YORK

PRENATAL bowing and angulation of a single tubular bone or of a pair of tubular bones have been reported in a small number of cases.[1] Congenital anterior curvature of one or both tibias, congenital tibial kyphosis, is the commonest and best known lesion of this type. Chapple and Davidson [2] described the case of a newborn infant who presented congenital symmetric lateral bowing of the femurs with bilateral dislocation of the hips; the remainder of the skeleton apparently was normal in this case, and the "position of comfort" assumed by the infant did not suggest faulty fetal position of the arms. Middleton [1b] observed associated bendings in the femoral shafts of a newborn infant, who also exhibited bilateral tibial kyphosis and talipes equinus. Concomitant deformities of the bones in the upper extremities, however, were not described in any of the patients who were reported to have congenital curved deformities in the bones of the lower extremities.

Included in this report are the case histories of 3 infants, each of whom had congenital symmetric bowings of the femoral and humeral shafts and similar, but sometimes unpaired, deformities of the shafts of the tibias, radiuses and ulnas. In each case the bowed diaphysial segments were thickened, as well as bent. All the curvatures extended through substantial longitudinal segments of the shafts in or near their middle thirds. Large, symmetric cutaneous dimples overlay the salient angles of the curves in several of the deformed bones.

From the Pediatric Department, Columbia University College of Physicians and Surgeons, and the Babies Hospital.

1. (*a*) Browne, D.: Congenital Deformities of Mechanical Origin, Proc. Roy. Soc. Med. **29**:1409, 1936. (*b*) Middleton, D. S.: Studies on Prenatal Lesions of Striated Muscles as a Cause of Congenital Deformity: I. Congenital Tibial Kyphosis; II. Congenital High Shoulder; III. Myodystrophia Fœtalis Deformans, Edinburgh M. J. **41**:401, 1934.

2. Chapple, C. C., and Davidson, D. T.: A Study of the Relationship Between Fetal Position and Certain Congenital Deformities, J. Pediat. **18**:483, 1941.

The cause and pathogenesis of the skeletal and cutaneous lesions have not been determined with certainty, but there is much evidence which suggests that they were caused by mechanical pressure in utero, operating on ectopic fetal extremities.

REPORTS OF CASES

CASE 1.—W. W., a Negro boy, was born of a healthy primiparous mother after a normal gestation and labor. His weight at birth was 2,950 Gm.; his total length was 48 cm.; the segment from the crown to the symphysis pubis was 31 cm. in length. Kahn tests on the blood serums of the mother and of the infant gave negative reactions for syphilis. At birth multiple symmetric bowings of the thighs, shanks, arms and forearms were evident. A photograph

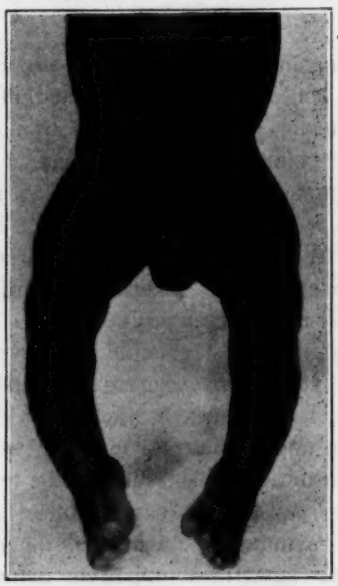

Fig. 1 (case 1).—Photograph of the lower extremities on the seventeenth day of life. The thighs and shanks are bowed laterad and, to a less degree, ventrad. Similar, but less conspicuous, deformities were present in the arms and forearms.

of these deformities on the seventeenth day of life is shown in figure 1. Clinical examination showed that the bowing deformities were much more conspicuous in the legs than in the arms. The general muscular tone was normal, and there was no evidence of muscular spasm or of contractions of the soft tissues on the concave side of the curvatures. The feet were not deformed. Roentgenograms made on the fourth day of life showed symmetric bowing deformities and thickenings of the femurs, humeri, radiuses and ulnas (fig. 2). The right tibia and the right fibula were not affected. Other tubular bones, such as the metacarpal and metatarsal bones, the ribs and the clavicle, were normal in shape, as were the flat bones of the skull, the shoulder girdles, the pelvis and the vertebral column.

Large, symmetric cutaneous dimples overlay approximately the summits of the curves in the tibias and fibulas and in the radiuses and ulnas. There was no dimpling of the skin at the sites of the curvatures in the femurs or in the humeri.

On the twenty-second day of life the hemoglobin content and the cellular components of the blood were normal. During the third month calcium and

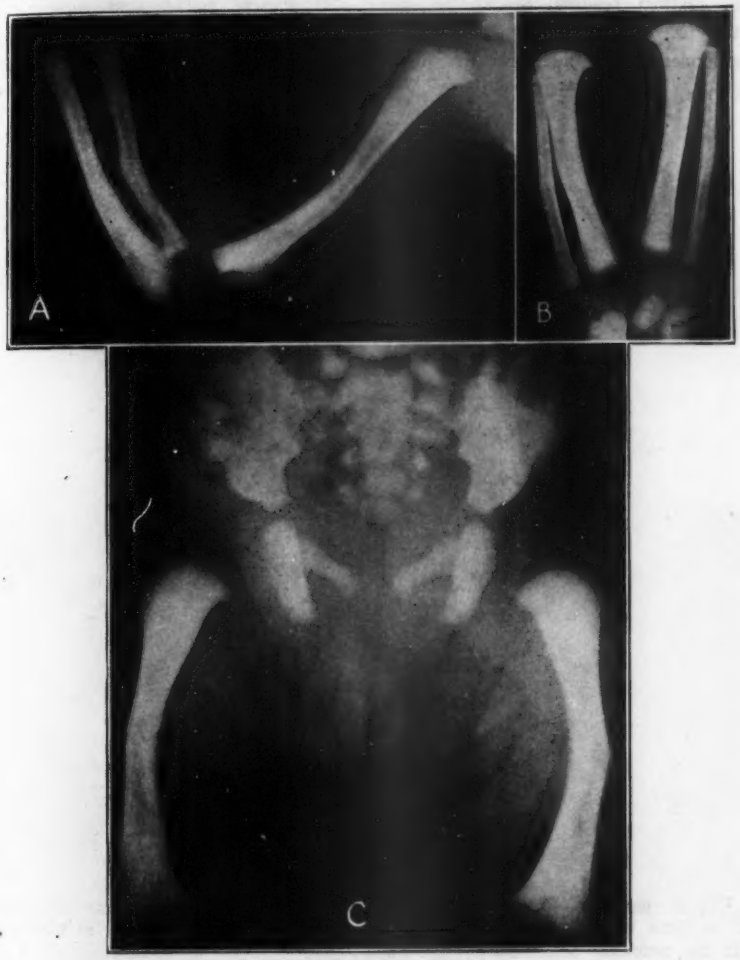

Fig. 2 (case 1).—Roentgenograms of the long bones on the fourth day of life. *A*, left upper extremity. In the middle thirds of the humerus and radius there are bowing deformities directed toward the extensor surfaces. The cortical segments on the concave sides of the curves are thickened. The ulna is only slightly affected. There were similar changes in the right upper extremity. *B*, right shank. The right tibia and fibula are bowed and show internal cortical thickening on the inside of the curves. The left fibula shows a short lateral bulge, but the left tibia is practically unaffected. *C*, pelvis and thighs in frontal projection. Both femurs are bowed and thickened, the left more than the right.

The magnitude of the various lesions indicates that the greatest compressing forces in fetal life were exerted on the right tibia and the left femur and the least on the left tibia.

phosphorus concentrations of the blood serum were normal, as was the phosphatase activity. Other than the deformities in the extremities and the dimples in the skin, there have been no significant clinical findings. Growth and development have progressed normally. The arms and legs have been moved freely since birth. The infant sat up at 7 months of age and stood alone at 1 year. The deformities of the extremities have diminished gradually since birth. However, distinct residual deformities were still present twenty-four months after birth (fig. 3). Roentgenograms made during the twenty-fourth month showed pronounced improvement in the bowings and the thickenings of the diaphyses (fig. 4). The large spurs on the medial aspects of the distal ends of the femurs

Fig. 3 (case 1).—Photograph of child at 2 years of age. Lateral bowings are still evident in the thighs and shanks, but they are all improved in comparison with the neonatal deformities (fig. 1).

and the proximal ends of the tibias are noteworthy; they were not present at birth and developed in the absence of rickets or tibial osteochondrosis infantilis (Blount's disease). In this patient they were probably caused by the mechanical stresses of postnatal muscular function and bearing of weight on the prenatally bowed bones. The anterior components of the bony curvatures in the lower extremities are shown in figure 5.

The cutaneous dimples persisted and were still conspicuous when the patient was last observed at 2 years of age (fig. 6).

CASE 2.—H. M., a Negro boy, was first examined when he was 17 months of age. He was born of a normal mother after a normal gestation and delivery with forceps. The weight at birth was 7 pounds (3,175 Gm.). His single sibling died at birth. Multiple bowing deformities of the legs and a deep dimple on the anterolateral aspect of the right shin were noted at birth, and these were said to have persisted without significant changes. The infant thrived on a normal diet, which contained adequate supplements of vitamins C and D. Save for the deformities, his development was normal, and he exhibited surprisingly little dis-

Fig. 4 (case 1).—Roentgenograms of the extremities at 2 years of age. *A*, arms; *B*, thighs, and *C*, shanks. The bowings and thickenings are diminished in all the bones as compared with earlier observations (fig. 2). The arrows are directed toward the large spurs on the medial aspects of the femurs and tibias; these spurs increased progressively with advancing age.

ability in view of the pronounced congenital deformities of the right lower extremity. He held his head erect at 5 months, sat alone at 7 months and began to walk at 12 months of age. A swelling appeared in the left groin during the sixth month; later, this was identified as an inguinal hernia, which was repaired surgically.

At the age of 17 months, the weight was 21 pounds (9,525 Gm.) and the length 29 inches (74 cm.). The legs were deformed (fig. 7), and the child walked with a limp, owing to the shortening of the right leg. The thighs were bowed laterad and, to a less degree, ventrad. The right shank, however, presented a pronounced ventral curvature, with relatively slight lateral bowing. On

Fig. 5 (case 1).—Lateral projection of the right leg at 11 months. The femur, tibia and fibula are bowed ventrad. The posterior cortical segments in the concave aspects of the curves are all thickened inwardly.

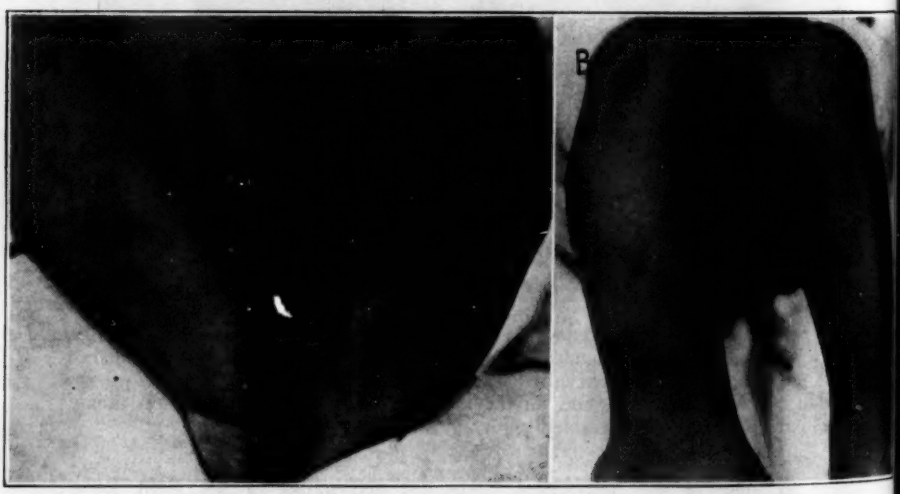

Fig. 6 (case 1).—Photographs of the extremities at 2 years. *A*, forearms; *B*, shanks. Large symmetric dimples mark the skin over approximately the salient angles of the underlying deformed bones. These dimples were present at birth and changed little with advancing age. In this patient there were no cutaneous dimples either on the thighs or on the proximal segments of the arms.

the apex of the bend in the right shin, on its anterolateral aspect, there was a deep cutaneous pit (fig. 8). The floor of the pit was adherent to the underlying bone, which was later demonstrated to be a bony knob projecting from the right fibula (fig. 10 *C*). The left shank was not deformed, and both feet were normal. Little, if any, deformity was noted in the arms in the physical examination, but

Fig. 7 (case 2).—Photographs of the bowed legs at 17 months of age. The arrow is directed toward a deep cutaneous depression on the bowed right shank.

Fig. 8 (case 2).—Photograph of the right shank at 17 months. The deep cutaneous pit on the anterolateral aspect of the right shank is shown in detail. The floor of this cutaneous lesion was adherent to a knoblike exostosis on the right fibula.

several large dimples marked the skin of the arms and the forearms (fig. 9). These dimples were symmetrically placed on the posterolateral aspects of the arms at approximately the summits of the bowing deformities later demonstrated roentgenographically in the humerus and the radiuses and ulnas (fig. 10 and 11).

The ribs, clavicles, scapulas, pelvic bones, skull and spine were all normal roentgenographically. Roentgenograms were also made during the twenty-ninth month of life; the findings in the bones of the lower extremities at this time were similar to those at the age of 17 months, but decided improvement was evident in the bones of the forearms (fig. 12).

At 18 months, tests for muscular function revealed no abnormalities; in particular, there was no sign of contraction in or shortening of the flexor groups of muscles on the concave side of the bony deformities. At this time constant nystagmus and myopia of the left eye were noted, which were thought to be of congenital origin. The hemoglobin content and the cells of the blood were normal. The serum calcium and phosphorus measured 9.9 and 7.8 mg. per hundred cubic centimeters, respectively, and the activity of the serum phosphatase equaled 48.5 Bodansky units. The urine was normal. The Kline test of the blood gave a negative reaction for syphilis, and there was no reaction to the cutaneous test with tuberculin. His clinical status had remained essentially unchanged when he was last examined, at 30 months of age. An orthopedic

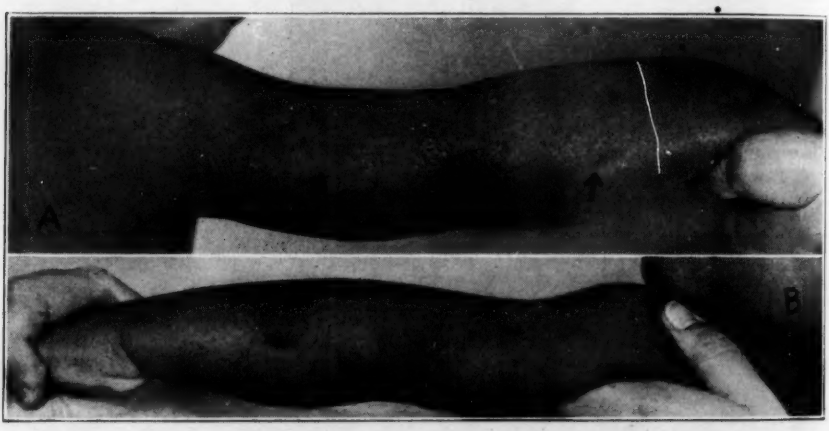

Fig. 9 (case 2).—Photographs of the upper extremities at 17 months. *A*, left; *B*, right. There are symmetric cutaneous dimples on the extensor aspects of both arms and both forearms. Of each pair of dimples, the one on the left side is deeper. Each dimple is superimposed approximately on the summit of the curve in the bone underlying it.

consultant advised observation without special therapy in the hope that a regression of the deformities would occur spontaneously; the opinion was also given, however, that the pronounced bowing of the right tibia would probably require osteotomy later.

Case 3.—A white boy was born of a normal primiparous mother after normal gestation and labor. He was a patient of Dr. Sidney S. Chipman, who furnished the clinical notes and roentgenograms. At birth there were pronounced bowing deformities of all the extremities, with some limitation in the movements of the left leg. The left shank was bowed laterad and ventrad. Roentgenograms of the extremities made on the fifth day of life disclosed symmetric bowings and thickenings of the tubular bones of the extremities (figs. 13 and 14). Bones in other parts of the body were not affected. The roofs of the acetabular cavities appeared to be hypoplastic, which suggested congenital dislocation of the hips,

but this diagnosis was not confirmed in later examinations. The infant grew and developed normally save for the deformities. He walked with support when 1 year of age. The curves in the humeri had disappeared by the tenth month and the lower extremities gradually became straighter, but conspicuous deformities were still present at the age of 20 months. An osteotomy of the left tibia was performed when the infant was 13 months of age. At the age of 7 years, all the deformities were said to have been greatly improved as compared with the neonatal and infantile status. Dimpling of the skin was not observed; it was not looked for specifically.

Fig. 10 (case 2).—Roentgenograms of the extremities at 17 months. *A*, right upper extremity. Bowings are present in all the bones; the curves are located in the middle thirds of the radius and ulna and in the lower third of the humerus. The convexities of the curves are directed toward the extensor surfaces at approximately the sites occupied by the cutaneous dimples shown in figure 9. *B*, thighs and hips. The femurs are bowed laterad in their middle thirds. *C*, shanks and knees. The right tibia and fibula appear to be approximately straight but are shortened. On the right fibula there is a knoblike exostosis; this is not made up of solid compacta but appears to be a protrusion of the medullary cavity and cortex laterad. The floor of the deep cutaneous pit (fig. 8) was adherent to this fibular knob.

Fig. 11 (case 2).—Lateral projections of the legs at 17 months. *A*, right; *B*, left. In this projection ventral bending of the shortened right tibia is evident, but the right fibula is straight. The exostosis in the right fibula projects ventrad (arrow).

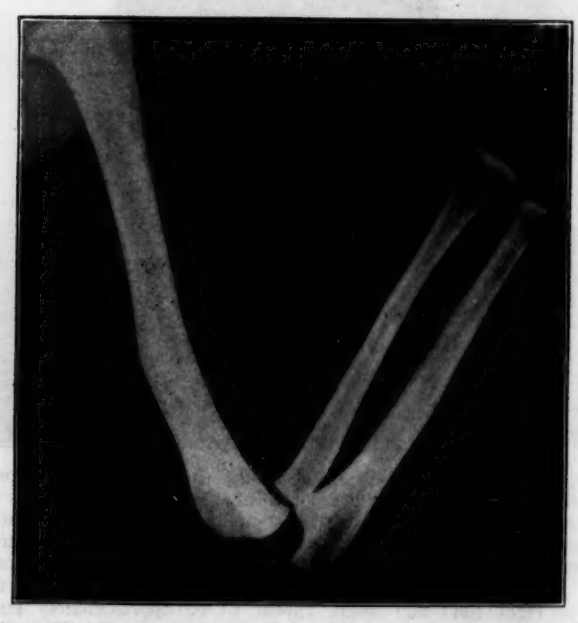

Fig. 12 (case 2).—Roentgenogram of the right arm at 29 months. As compared with figure 10 *A*, the deformities previously present in the radius and ulna have disappeared; the humeral bowing, in contrast, is still evident in the lower third of the shaft.

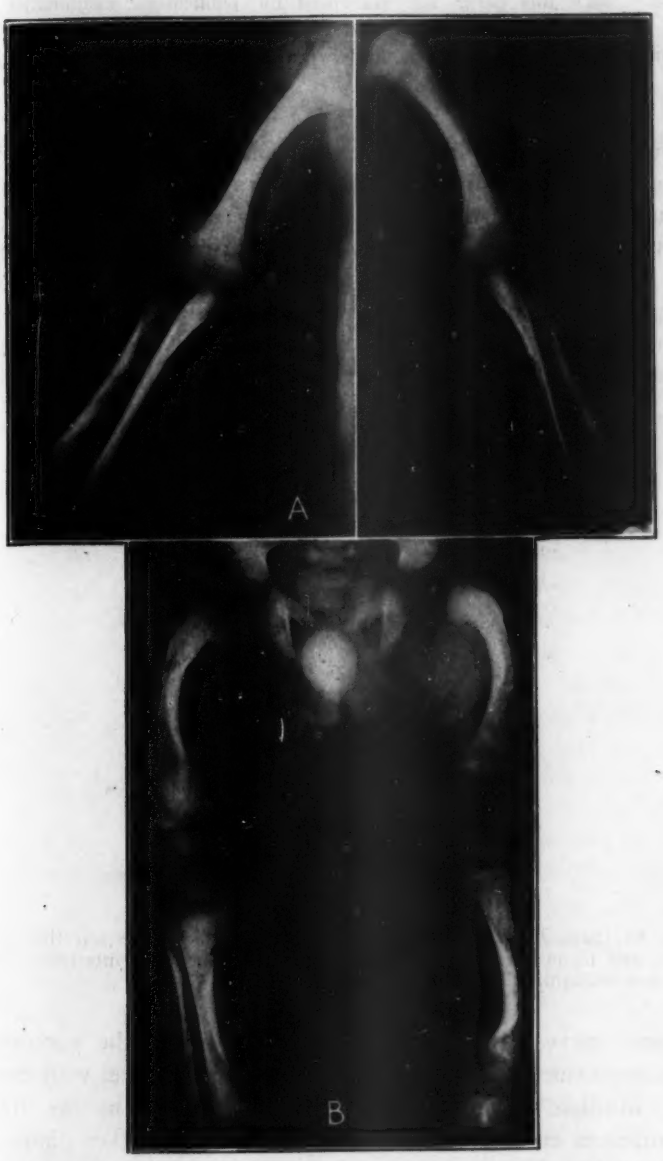

Fig. 13 (case 3).—Roentgenograms of the extremities on the fifth day of life. *A*, and *B*, upper and lower extremities, respectively. *A*, the middle thirds of the humeral shafts are bowed and thickened in a fashion similar to that of the humeri of the first patient on the fourth day of life (fig. 2). Shallow, asymmetric curvatures are evident in the radiuses and ulnas. *B*, the femurs and the tibias are bowed laterad, and the compacta in the inside of the curves is thickened internally, with corresponding decrease in the volume of the medullary cavities. The right fibula is little affected, while the left fibula presents a double curve with internal cortical thickening on the concave side of each of its two curves.

NOTE.—Since this paper was submitted for publication, examination of the patient at the age of 7 years showed residual bowing deformities, and cortical thickenings were still visible in the left tibia and in both femurs (roentgenograms).

COMMENT

Certain positive findings were common to these 3 cases. Multiple bowing deformities of the tubular bones of the extremities were present at birth, and the nature and magnitude of the skeletal lesions suggested that they had been developing during a long period prior to birth. Symmetric lateral bowings of the femurs and symmetric posterior bowings of the humeri characterized each case. Distal to the knees and the elbows, however, the deformities of the bones were usually not symmetric. At birth, the cortical segments on the concave sides of

Fig. 14 (case 3).—Lateral projection of the shanks. The left tibia is bowed ventrad, and its posterior concave cortical wall is thickened internally. Both the fibulas are straight.

the bony curves were thickened inwardly while the corresponding cortical segments on the convex sides of the same curves were unusually thin. Multiple cutaneous dimples were present in the deformed extremities in cases 1 and 2. It is not certain whether dimples were present or absent in case 3. Satisfactory serial observations were made only in case 1; after the birth of the patient, both the bony curvatures and their cortical thickenings slowly regressed, and some of them had disappeared entirely by the twenty-fourth month.

There were also many significant negative features. The infants were born of healthy mothers, and there was no evidence of inherited or familial skeletal or cutaneous disease. The infants themselves

were healthy except for the deformities and the disabilities due to the deformities. In each case the skeletal lesions were confined to the long tubular bones of the limbs; the bones of the hands, feet, head, thorax, pelvis and spine were not affected. Morbid changes were not demonstrated, save in the skeleton and in the skin. Endochondral bone formation had apparently progressed normally, as judged from the roentgenographic observations on the metaphyses and epiphyses of the affected and unaffected bones. There was no evidence of any of the intrinsic prenatal skeletal dysplasias which cause deformities in the long bones of the fetus, such as achondroplasia or dyschondroplasia. There were also no roentgenographic signs of the diseases in which prenatal fractures are commonly found, such as fragilitas ossium (osteogenesis imperfecta) or pseudarthrosis. There was no clinical, roentgenographic or serologic evidence of prenatal or infantile rickets or syphilis. It should be emphasized that the deformities were distinctly regional, often symmetric, and were not generalized.

The cause and pathogenesis of these prenatal deformities cannot be established by direct observation, and it is unlikely that they will be unless new methods of examination are introduced for their study. There are, however, many findings which offer convincing indirect evidence in support of the hypothesis that the bony lesions resulted solely from mechanical disturbances in utero, secondary to elocation of the fetal arms and legs. The skeletal deformities can be explained satisfactorily in large part by assuming that the fetal arms and legs were packed in attitudes which permitted the transmission of deforming uterine pressures from one impacted fetal part to another. In like fashion, pressure from the uterine wall on the fetal skin compressed on ectopic, exposed bony points of the fetus produced the cutaneous dimplings.

Other theories of the causation of such lesions are meager, and none of them is tenable in these cases. Middleton [1b] postulated undergrowth in length of the flexor muscles of the calf to explain anterior tibial kyphosis; this hypothesis does not fit the present cases, because at birth there was no sign of muscular shortening or of the secondary deformities characteristic of muscular shortening, such as talipes equinus —conditions which were present in Middleton's cases of tibial kyphosis and on which he based his principal arguments. It is, of course, possible that the transient muscular shortening of early fetal life produced curvatures of bone which persisted long after the muscular shortening had disappeared.

Multiple angulations of the shafts due to prenatal fractures secondary to pseudarthrosis can be easily excluded; none of the cardinal signs of pseudarthrosis, such as focal degeneration of the bone, pathologic frac-

ture or false motion at the site of the diaphysial angulation,[3] was evident. Traction on the fetal extremities by amniotic adhesions or constrictions by the umbilical cord need not be considered as causal factors because these agents supposedly never cause lesions proximal to the elbows and knees. Since Streeter's investigation of fetal amputations,[4] amniotic adhesions and constriction by the umbilical cord have been generally discredited as pathogenetic factors in fetal deformities. Arthrogryposis (amyoplasia congenita) is complicated with congenital malformations of the extremities, but this condition was manifestly not present in these patients because their muscular development was normal.

The cutaneous dimples, the bowing of the long bones and the cortical thickening in the curved segments of the bones are all consonant with the hypothesis of simple mechanical molding of the displaced fetal arms and legs. According to Browne,[1a] ectopic dimples are stigmas of fetal compression. They develop in the fetal skin in the sites of points of pressure between the maternal uterine wall and the superficial, sharp bony prominences of the fetal skeleton. The cutaneous depressions represent localized pressure atrophy of the subcutaneous soft tissues caught between the overlying uterine wall and the underlying bony prominence of the fetus.

According to this concept, cutaneous dimples should not develop over bony prominences buried deep in soft tissues or over superficial, poorly covered bony prominences not in close contact with the uterine wall. In cases 1 and 2 there were no dimples in the thighs, notwithstanding the symmetric bowings of the femurs in both patients, probably because the femoral prominences were sheltered by the thick, soft tissues which surround the femurs and prevent direct pressure by the uterine wall. The presence of symmetric dimples over the bowed humeri in case 2 and their absence from the same sites in case 1 are more difficult to explain. In the latter case one must assume, according to theory, that the summits of the humeral curves were not in contact with the uterine wall, or that they were in contact with it but were protected from direct pressures of the uterine wall by thicker pads of soft tissue than in case 2. In case 1 there was little, or no, regression of the dimples with advancing age; in case 2 the dimples were large and conspicuous both at the seventeenth month, when the child was first examined, and later, during the thirtieth month.

It is self evident that the bowings of the tubular bones present at birth could have been caused by mechanical bending forces to which these bones were subjected long before birth, probably at first during an

3. Williams, E. R.: Two Congenital Deformities of the Tibia: Congenital Angulation and Congenital Pseudarthrosis, Brit. J. Radiol. **16**:371, 1943.

4. Streeter, G. L.: Focal Deficiencies in Fetal Tissues and Their Relation to Intra-Uterine Amputation, Contrib. Embryol. **22**:1, 1930.

early phase of fetal life, when these bones were largely cartilaginous and more easily bent. The shape and the mode of growth of a tubular bone are based on an inherently determined form and are not dependent on the particular environment of the bone.[5] Abnormal fetal position alone does not explain the skeletal deformities; one must postulate an abnormal fetal posture in each case, one in which compressing forces were applied to the deformed bones at the sites of their concavities. The lesions of bone common to all 3 cases were the symmetric lateral bowings of the femurs and the symmetric dorsal bowings of the humeri. The deviation from the normal fetal position required to explain these skeletal mal-

Fig. 15.—Schematic drawing of the presumptive faulty fetal position common to the 3 patients. *A*, normal fetal position. *B*, presumptive fetal position responsible for bowings in the humeri and femurs observed in all 3 patients. Each hand impinges on its opposite humerus, and each foot impinges on its opposite femur in a fashion which probably permitted the force of the uterine muscle to be transmitted through the impinging part and produce the lateral bowings in the femurs and the posterior bowings in the humeri. The asymmetric deformities distal to the elbows and knees were probably due to variable patterns of intrauterine packing and folding of the shanks and forearms in each case.

formations need be only a slight one. The fetal extremities need only be folded into a cross leg and cross arm pattern, in which each foot presses on the internal aspect of its opposite thigh and each hand impinges on the flexor surface of its opposite upper arm (fig. 15). It is obvious from the roentgenograms that the fetal position of the shanks varied more than that of the thighs and the arms. It is probable that in

5. Brash, J. C.: Some Problems in Growth and the Developmental Mechanics of Bone, Edinburgh M. J. **41**:305 and 363, 1934.

each case the tibia with the more pronounced bowing and thickening was folded over the other tibia. In case 1 the right shank was more affected than the left; in case 2 there was severe anterior tibial kyphosis on the right, while the left tibia was normal, and in case 3 the left tibia was bowed laterad and ventrad and the distal ends of the left tibia and fibula were twisted. These variations are readily explained by assuming that the shanks were in slightly different fetal positions (fig. 16). The mild differences in the deformities in the radiuses and ulnas among patients and the paired differences in the same patient can be explained by putting the various pairs of crossed forearms into different degrees of pronation and supination.

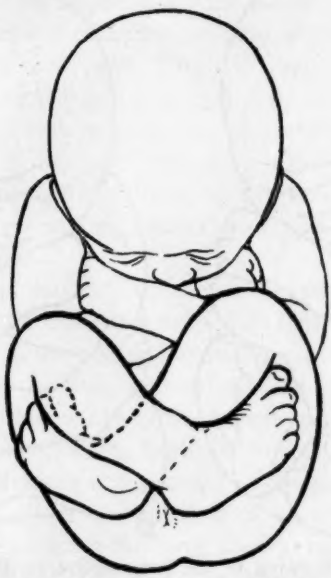

Fig. 16.—Schematic reconstruction of the probable malposition of the legs in case 2 which was responsible for the anterior tibial kyphosis on the right side. The right shank is folded over the left shank. The ventrolateral bowing of the left tibia in case 3 was probably caused by similar malposition, but with the left shank folded over the right one. Likewise, in case 1 the right shank probably was folded over the left, because the left tibia is much more deformed than the right.

At birth, a striking feature of every one of the bowed bones is the thickening of the cortical segment on the concave wall of the curve and the thinning of the opposite cortical segment on the convex wall of the curve (fig. 17 also figs. 2, 13 and 14). These cortical thickenings are all limited to the curve itself, and all are directed inward; the caliber of the contiguous medullary cavity is correspondingly reduced. It is clear that this cortical hypertrophy represents accretion due to failure of absorption of the cortex from within and, on the other hand, does not represent subperiosteal accretion on the external cortical surface. This

combination of cortical thickening on the concavity and cortical thinning on the convexity is, in my opinion, another example of structural adaptation of the affected bones to prenatal extraskeletal forces of compression which operated at the sites of the cortical thickenings. Figure 18 depicts the probable pattern of the forces and their effect on a tubular bone. The principal forces involved are all derived from the muscular action of the uterine wall. Jansen [6] stated that functional muscular pressures operating on the sides of a growing bone cause formation of bone tissue, both spongy and compact, in the direction of that pressure; tensile forces, in contrast, never stimulate the formation of bone. The lesions in the present cases fit this concept of their genesis very well.

Fig. 17.—Drawing of the roentgenogram of the left shank in case 3, showing the cortical changes in detail. There is a single curvature in the tibia, and the cortical segment in the concavity of the curve is thickened, in contrast to the thinned-out cortical segment in the convex wall. The medullary cavity is greatly reduced in volume in the curved segment. The fibula presents a double curve, and in each curve the concave cortical wall is thickened, while the convex wall opposite is thin.

The gradual postnatal regression of the bowings of the bones and of the cortical thickenings also bespeaks structural adaptation of the bone to disturbed fetal mechanics. This regression was clearly evident in the first case, in which serial roentgenographic examinations were made from birth to the twenty-fourth month (fig. 19, also figs. 2 and 4). It is

6. Jansen, M.: On Bone Formation: Its Relation to Tension and Pressure, London, Longmans, Green & Co., 1920.

assumed that the release at birth from the compressing intrauterine forces permitted gradual restoration toward more normally shaped bones. In case 2 deformities in the radiuses and ulnas present at the seventeenth month had disappeared at the twenty-seventh month, although deformities in the other affected bones persisted.

The metaphysial spurs on the medial aspects of the opposing bones at the knees in cases 1 and 2 are noteworthy (figs. 4 and 10) because they developed in the absence of rickets and tibial osteochondrosis (Blount's disease[7]). The presence of bowed legs and crooked, thickened bones with tibial and femoral spurring in these cases as late as two years after birth demonstrates that the late infantile clinical and

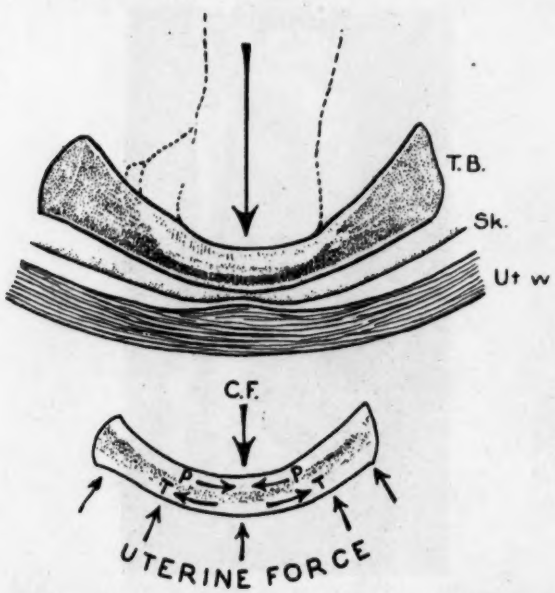

Fig. 18.—Schematic drawing of the forces of pressure and tension and their relation to the bowing and thickening of the affected bones. The heel transmits the compressing force to the tubular bone, which is bowed at the site of impact and the cortex of whose concave wall is thickened. The cortex on the convex wall of the curve is, in contrast, unusually thin. The skin caught between the summit of the bony curve and the uterine wall undergoes pressure atrophy, which produces a dimple. The diagram shows the direction of the opposing forces: *C.F.*, compressing force of the fetal part; *P*, pressure in the near wall of the tube; *T*, tension in the far side of the wall of the tube; *T.B.*, tubular bone; *Sk.*, fetal skin, and *Ut.W.*, uterine wall.

roentgenographic changes residual to prenatal mechanical bowing closely resemble the deformities of healed early infantile rickets. This type of nonrachitic bowed legs could easily be mistaken for rachitic bowed

7. Blount, W. R.: Osteochondrosis Deformans Tibiae, J. Bone & Joint Surg. **19**:1, 1937.

legs, especially when no cutaneous dimples are present or their presence is interpreted improperly. It is also probable that some of the cases which have been reported as instances of infantile tibial osteochondrosis were actually examples of prenatal bending of the bones in the legs. One should be cautious in the diagnosis of infantile tibial osteochondrosis, unless necrosis of the medial tibial condyle is associated with bowing and medial spurring of the tibias and femurs.

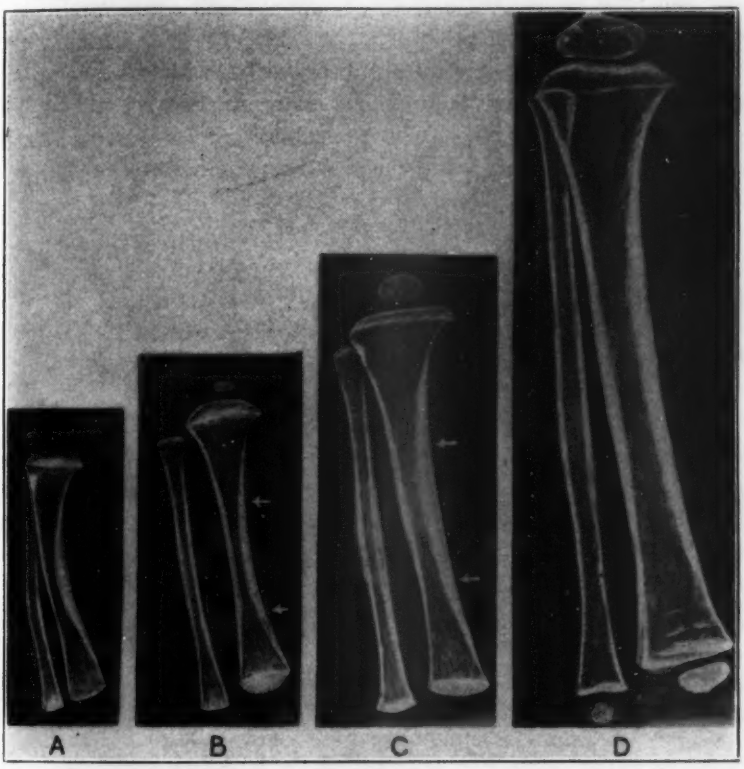

Fig. 19.—Gradual regression after birth of the curvature and the cortical thickening in the right tibia in case 1 (drawing of roentgenograms). *A*, on the fourth day of life. Prenatal lateral bowing, internal cortical thickening and stenosis of the medullary cavity are all evident. *B*, at 8 weeks of age. As compared with the condition in A, the tibial curve is much shallower; the cortical thickening is narrower and the medullary cavity wider. The cortical thickening has been reduced by excessive resorption from its internal surface, and, *pari passu*, the concavity of the arch has been partially filled in externally by the accretion of new peripheral cortex on the outside, beneath the periosteum. The external accretion is demonstrated by the fine external layer of new bone now bridging the inside of the curve. The convexity of the curve apparently has been straightened by a reverse process, namely, external cortical resorption and internal cortical thickening due to failure of normal resorption. This process is a beautiful example of the factors which operate to remodel a deformed bone during early life. *C*, and *D*, at 7 and 24 months, respectively. The forces of remodeling have apparently continued, and, as a result, at 2 years of age the normal shape of the tibia and a proper proportion of cortex and medullary cavity have been restored. The medial spurs on the proximal ends of the tibial shafts increased with advancing age, owing to the new postnatal mechanical stresses which operate in this part of the bowed bone.

SUMMARY

The clinical and roentgenographic findings in 3 cases of prenatal bowing and thickening of the tubular bones with multiple dimpling of the skin of the extremities are described.

Prenatal mechanical molding of the bones and pressure atrophy of the fetal skin are offered as the probable pathogenetic mechanisms.

The similarity of bowed legs caused by prenatal molding and the bowed legs due to rickets and to Blount's tibial osteochondrosis is emphasized.

Many of the bony deformities disappeared with advancing age, especially in the upper extremities, but many others were still present during the third year of life. All the neonatal dimples persisted during infancy without significant change with advancing age.

Babies Hospital (32).

TOTAL AND FRACTIONAL BLOOD LIPID LEVELS IN DISEASES OF CHILDHOOD

ELAINE M. THOMAS, M.D.
CHICAGO

THE LITERATURE contains a number of studies concerned with abnormalities of the blood lipids in various childhood diseases. However, with rare exception these studies do not take into account the entire blood lipid complex. Recent advances in the physiology of normal lipid metabolism emphasize the need for information with regard to the levels of all the blood lipids and such ratios as may exist among them.

The following report presents the total and fractional plasma lipid levels in 50 children with diseases which are classified diagnostically in table 1. Systematic investigation of changes produced by these diseases in the complete blood lipid pattern is the point of emphasis in this study.

PROCEDURE

Postabsorptive total and fractional plasma lipid levels were obtained in 50 children with the diseases indicated in table 1. The technics of Bloor [1] for the fractionation and the differential analysis of plasma lipids were employed. The following lipids were (with a few exceptions) determined for each child: total lipid,[2] phospholipid, total cholesterol, ester cholesterol, free cholesterol,[2] cholesterol ester fatty acid [2] and neutral fat.[2]

The major analytic procedures were: (1) alcohol-ether extraction of the lipids from plasma, (2) separation of the acetone-insoluble phospholipids from the remaining lipids by acetone precipitation, (3) oxidative determination (dichromate oxidation with heat) of the phospholipid and acetone-soluble fractions, the sum of which equals the total lipid, and (4) determination of total and ester cholesterol, using digitonin precipitation to remove free cholesterol in the latter analysis. In both cholesterol determinations, color was developed with the Liebermann-Burchard reagent and was read on the Coleman photoelectric colorimeter.

Control determinations were made of the total and fractional lipid levels of 24 healthy children living under normal conditions of diet and activity.

1. Bloor, W. R.: J. Biol. Chem. **24**:227, 1916; **77**:53, 1928; **82**:273, 1929.
2. Calculated values. Fatty acid is abbreviated as F.A. in the charts.

TABLE 1.—*Total and Fractional Plasma Lipid Levels in Diseases of Childhood*

Disease	Case Number	Determination	Total Lipid *†	Total Cholesterol *	Ester Cholesterol *	Free Cholesterol *†	Cholesterol Ester *	Cholesterol Ester Fatty Acids *†	Phospholipid *	Neutral Fat *†	Ester Cholesterol : Total Cholesterol	Phospholipid : Total Cholesterol
Nephrosis	1	1	1,885	860	575	285	975	400	375	250	0.67	0.43
		2	2,610	1,045	775	270	1,340	565	510	465	0.74	0.49
		3	6,800	2,020	1,170	850	2,025	855	785	3,150	0.58	0.39
		4	5,435	1,445	775	670	1,320	545	940	2,505	0.54	0.65
		5	3,100	935	600	335	1,040	430	670	1,065	0.64	0.71
		6	5,550	1,660	995	665	1,720	725	970	2,165	0.60	0.59
		7	5,185	1,610	1,035	575	1,790	755	850	1,970	0.64	0.52
		8	1,435	610	450	160	780	330	370	125	0.73	0.60
	2	1	6,070	1,295	1,040	255	1,800	760	790	3,225	0.80	0.61
		2	1,780	555	255	300	440	185	460	580	0.46	0.83
	3	..	2,175	920	650	270	1,125	475	510	270	0.70	0.55
	4	1	1,585	535	375	155	650	275	385	410	0.70	0.72
		2	1,945	310	165	145	285	120	405	1,110	0.53	1.35
Chronic glomerulonephritis (minimal edema)	5	..	1,155	465	345	120	595	250	265	175	0.74	0.57
	6	..	980	410	300	110	520	220	215	135	0.73	0.52
Pyelonephritis	7	..	740	270	160	110	275	115	220	135	0.59	0.81
Hyperthyroidism	8	1	620	250	165	85	285	120	175	75	0.66	0.71
		2	510	160	95	65	165	70	130	150	0.59	0.81
	9	..	620	185	110	75	190	80	155	200	0.59	0.84
Hypothyroidism	10	1	1,375	650	475	175	830	345	360	30	0.73	0.55
		2	690	255	175	80	300	125	205	105	0.69	0.80
		3	1,090	505	345	160	505	250	245	30	0.68	0.48
		4	1,110	500	335	165	580	254	275	90	0.67	0.55
		5	1,195	470	380	90	655	290	270	160	0.80	0.57
		6	1,335	620	445	175	770	325	335	55	0.72	0.54
		7	795	265	180	85	310	130	220	180	0.68	0.83
		8	940	385	280	105	485	205	255	95	0.75	0.67
	11	1	1,130	335	225	110	390	165	335	295	0.67	1.00
		2	460	135	80	55	140	60	150	115	0.59	1.10
		3	1,025	195	130	65	225	95	240	495	0.67	1.25
		4	1,225	400	270	130	465	195	345	285	0.67	0.86
		5	635	215	130	85	225	95	200	125	0.60	0.93
Treated	12	..	535	185	165	20	285	120	140	90	0.89	0.76
Untreated	13	1	1,010	...	...	...	...	...	250	...	....	....
Treated		2	730	280	160	120	275	95	155	180	0.57	0.55
Hypothyroidism	14	1 ‡	800	350	225	125	390	165	230	145	0.64	0.66
		2 §	595	240	120	120	200	75	165	105	0.50	0.68

Hepatic disease												
Subacute catarrhal hepatitis	15	1	790	190	70	120	120	...	260	290	0.37	1.37
		2	635	130	36	95	60	...	220	260	0.28	1.70
		3	695	255	160	95	275	...	165	160	0.63	0.65
Congenital biliary stenosis with cirrhosis	16	..	770	290	185	105	310	...	260	85	0.64	0.80
Idiopathic hepatosplenomegaly	17	..	700	265	160	105	277	...	215	105	0.80	0.81
Xanthomatous biliary cirrhosis	Adult	..	2,925	910	180	730	310	...	1,255	630	0.20	1.40
Diabetes mellitus	18	..	765	270	210	60	365	...	290	50	0.78	1.75
	19	..	780	300	230	70	400	...	245	65	0.77	0.81
	20	..	625	185	60	125	105	...	260	135	0.33	1.40
	21	..	570	...	...	...	...	...	170	...	....	....
	22	..	765	270	...	...	310	...	210	...	....	0.77
	23	1	750	290	190	100	330	...	280	90	0.65	0.79
		2	755	255	155	100	270	...	220	165	0.61	0.86
	24	..	865	295	195	100	335	...	285	150	0.66	0.96
	25	..	...	280	215	65	370	...	...	145	0.77	....
Glycogenosis	26	1	4,805	410	175	235	300	...	605	3,665	0.42	1.47
		2	7,960	795	360	435	625	...	1,480	5,420	0.45	1.86
		3	2,570	165	90	75	155	...	555	1,785	0.54	3.36
Nutritional disturbances												
Malnutrition	27	..	565	200	110	90	190	...	155	130	0.55	0.77
Malnutrition	28	..	695	180	90	90	155	...	175	275	0.50	0.97
Malnutrition	29	..	495	150	110	40	70	...	210	75	0.73	1.40
Malnutrition with bronchial asthma	30	..	380	150	...	..	...	...	120	..	....	....
Carotenemia	31	..	1,030	365	265	100	460	...	335	135	0.72	0.91
Pancreatic cystic fibrosis	32	1	385	120	85	35	145	...	125	90	0.71	1.04
		2	415	145	110	35	190	...	140	50	0.76	0.97
		3	345	...	...	..	...	...	75	..	....	....
Juvenile obesity	33	..	455	190	...	..	...	...	130	...	....	0.68
	34	..	795	350	...	..	...	...	170	...	....	0.49
	35	..	535	...	70	..	120	...	150	..	....	....
	36	..	605	205	140	65	240	...	230	70	0.68	1.10
	37	..	1,120	220	110	110	190	...	290	530	0.50	1.31
Rheumatic fever	38	..	780	275	235	40	405	...	225	105	0.85	0.81
	39	..	620	250	150	100	260	...	155	105	0.60	0.62
	40	..	720	265	195	70	335	...	195	120	0.74	0.73
	41	..	720	270	180	50	310	...	210	150	0.67	0.77
	42	..	675	245	170	75	295	...	190	115	0.70	0.77
	43	..	655	230	165	65	285	...	255	50	0.65	1.10
	44	..	645	...	...	..	...	...	160	..	....	0.56
	45	..	590	245	160	85	280	...	145	80	0.65	0.89
	46	..	615	215	150	65	260	...	145	145	0.70	0.67
	47	..	635	225	165	60	285	...	145	145	0.73	0.64
	48	..	780	310	215	95	360	...	205	120	0.60	0.66
Rheumatoid arthritis	49	..	615	240	155	85	270	...	145	110	0.64	0.60
	50	..	430	165	85	80	145	...	110	95	0.51	0.66

* Mg. per hundred cubic centimeters.
† These are calculated values, see text.
‡ Patient received unsupervised home treatment; probably inadequate.
§ Patient treated in hospital two weeks.

RESULTS

Table 2 summarizes the levels of, and certain ratios among, the blood lipids of the 24 normal children, grouped according to age (6 to 14 years). Ranges and mean values for the group as a whole are included.

All of the lipids of the children in this group show wide individual variations. No relation to age is apparent. This is in general accord with previous observations in children,[2] as well as in adults.

TABLE 2.—*Blood Lipid Values in Normal Children* *

Age, Years	Total Lipid †	Phospho-lipid	Total Choles-terol	Ester Choles-terol	Ester Cholesterol : Total Cholesterol	Free Choles-terol	Neutral Fat
6-7	680	235	225	155	0.69	100	80
	545	185	200	155	0.77	45	45
	645	145	215	155	0.72	55	95
8	725	235	260	120	0.46	140	145
	625	245	185	...	....	...	...
	755	185	180	115	0.64	65	305
9	590	200	190	150	0.79	40	90
	605	210	280	145	0.63	85	60
	480	165	190	120	0.63	70	40
	620	185	235	140	0.60	95	100
10	545	135	215	115	0.53	100	100
	550	160	190	110	0.57	80	120
	685	155	275	190	0.69	85	115
	570	150	250	150	0.60	100	60
11	630	185	225	170	0.75	55	95
	745	265	160	110	0.69	40	250
12	670	225	...	...	....	...	...
	750	190	275	235	0.86	40	115
	535	155	210	135	0.64	75	70
13	665	265	190	135	0.71	55	115
	530	150	165	105	0.64	60	140
	650	195	185	110	0.59	75	195
	550	150	195	150	0.77	45	95
14	525	180	130	75	0.58	55	160
Range	480-755	135-265	130-275	75-255	0.46-0.86	40-140	40-305
Mean	620	190	210	140	0.70	70	120

Average ratio, phospholipid : total cholesterol..... 0.9
Average ratio, total cholesterol : total lipid..... 0.33
Average ratio, phospholipid : total lipid..... 0.30
Average ratio, ester cholesterol : free cholesterol..... 2.25

† Lipid values are stated in milligrams per hundred cubic centimeters of plasma.

* All values stated to nearest 5 mg.

It was noted that the mean cholesterol values here obtained agreed closely with those observed by Hodges, Sperry and Andersen [3] in their study of 417 normal children ranging in age from 2 months to 13 years. These investigators obtained a mean total cholesterol of 205 mg., and a mean ester cholesterol : free cholesterol ratio of 2.58 (Schoenheimer

3. Hodges, R. G.; Sperry, W. M., and Andersen, D. H.: (*a*) Serum Cholesterol Values for Infants and Children, Am. J. Dis. Child. **65**:858 (June) 1943; (*b*) J. Biol. Chem. **106**:745, 1934.

and Sperry technic [4]) for the determination of free and combined cholesterol in 417 normal children ranging in age from 2 months to 13 years.

In table 1 are summarized the total and fractional lipid levels in the plasma of the 50 patients.

Wherever the number of cases of a given disease justifies comment, the following characteristics of its lipid pattern are considered: (*a*) direction and degree of abnormal change in the total lipid level and in the individual lipids, (*b*) the relative importance of specific lipids in producing the total lipid alteration and (*c*) changes in certain important ratios.

COMMENT

Chronic Renal Disease.—Chart 1 illustrates the lipid patterns obtained in 7 cases of chronic renal disease, namely, high lipid levels in 4 patients

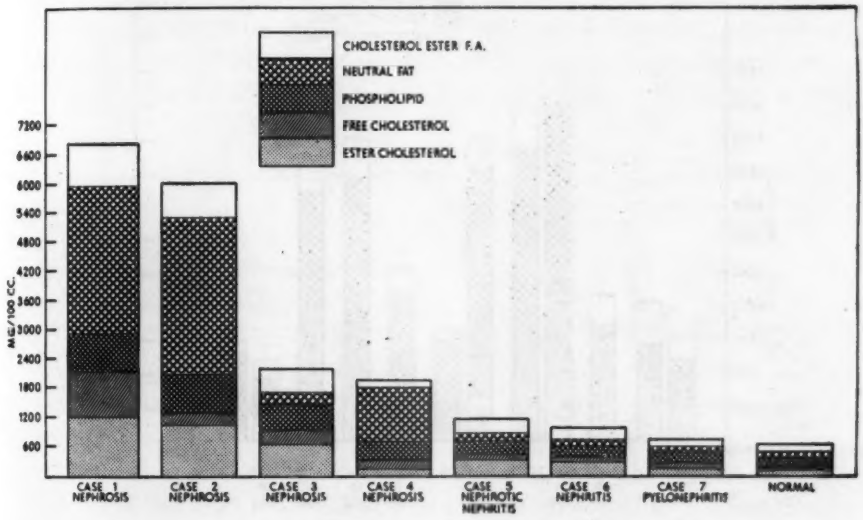

Chart 1.—The high lipid levels in 7 children with chronic renal diseases. The last column to the right represents normal lipid values.

with active nephrosis, more moderate elevations in 2 patients with chronic glomerulonephritis who did not display the nephrotic syndrome and normal levels in a patient with pyelonephritis.

Chart 2 shows variations in the plasma lipid pattern in a patient with nephrosis (case 1). This patient's lipid levels were studied during a nine month period when the disease was active and were reevaluated after the disease had been quiescent for six months. Cases 2, 3 and 4 are included in the chart for comparison.

It will be observed that the total and fractional lipid levels in case 1 fluctuated greatly during the course of the disease. The maximal levels occurred during periods of increasing edema.

4. Schoenheimer, R., and Sperry, W. M.: J. Biol. Chem. **106**:745, 1934.

In the accompanying tabulation (table 3), attention is directed to the following points: (*a*) the high percentage of neutral fat in the severe stage of the illness as contrasted with the low values for neutral fat during the mild and quiescent stages, and (*b*) the preponderance of cholesterol over neutral fat in the mild quiescent stages. Lability of neutral fat greater than that of phospholipid or of cholesterol and independent of variations in the cholesterol level has been reported in nephrotic adults.[5]

In the series of eight determinations in case 1, the ratio of ester to total cholesterol fell slightly as the total lipid level rose, returning to normal in the sample taken during convalescence. Though the afore-

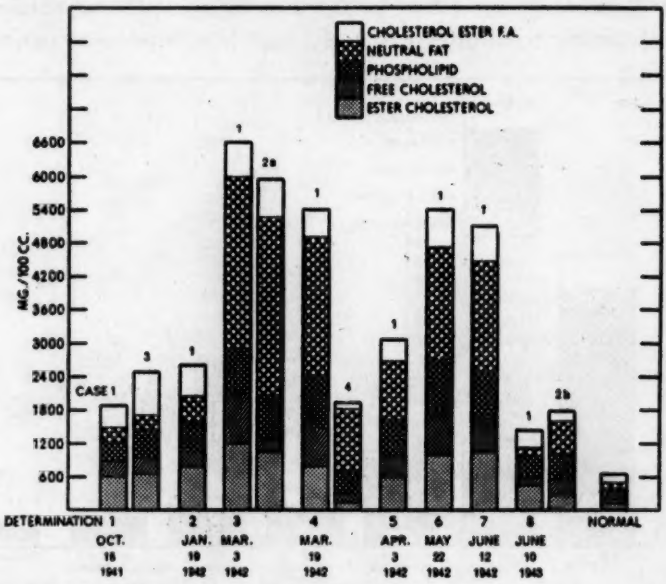

Chart 2.—Variations of the plasma lipid levels in a patient with nephrosis (case 1). Levels in other patients (cases 2, 3 and 4), as well as normal values, are included for comparison.

mentioned ratios were within the normal range, the apparent occurrence of a shift calls for further study of this point.

Cholesterol was chiefly responsible for the total lipid elevation in the 2 cases of moderately severe chronic glomerulonephritis with minimal edema (cases 5 and 6). Significant increase in neutral fat did not occur.

Diseases of the Thyroid Gland.—In 2 girls, 11 years of age, with severe hyperthyroidism (cases 8 and 9) all lipid levels were within the

5. (*a*) Page, I. H.; Kirk, E., and Van Slyke, D. D.: J. Clin. Investigation **15**:101, 1936. (*b*) Peters, J. P., and Man, E.: ibid. **22**:721, 1943.

normal range, though low normal in the second determination in case 8. Peters and Man [6] reported lowering of cholesterol and lipid phosphorus in adults with hyperthyroidism.

In 4 untreated or poorly treated patients with hypothyroidism, elevated total lipid levels were obtained. One adequately treated child had normal levels (case 12).

Chart 3 illustrates variations in the lipid levels of 2 children with cretinism (cases 10 and 11) over a three month period under conditions indicated in the accompanying table (table 4). The first patient (case 10) had received little thyroid at any time and none at all for a month; the second patient (case 11) had never been treated. The maximal total lipid elevations of these 2 children, moderate by contrast with those in nephrosis, resemble those obtained by Radwin [6a] in a group of 17 children with hypothyroidism. (Radwin, using the gravimetric method of Page, Kirk and Van Slyke [5a] for total lipids, obtained a mean normal value of 614 mg. per hundred cubic centimeters, which is almost identical with the mean normal in the present series.) As shown in the

TABLE 3.—*Percentage of Total Lipid Increase*

	Increase Due to Cholesterol (%)	Increase Due to Neutral Fat (%)	Increase Due to Phospholipid (%)
Determination 1 (early, mild stage)	50	10	13
Determination 2 (severe stage)	29	46	9
Determination 3 (quiescent stage)	47	0	17

accompanying tabulation (table 5), the first patient (case 10) had a greater relative cholesterol elevation, and a smaller relative neutral fat elevation, than did the second patient (case 11). These differences were evident whenever elevations occurred during the observation period. The ratio of ester to total cholesterol remained normal throughout.

Peters and Man [6] in studying adults with hypothyroidism likewise noted individual differences in the degree of neutral fat elevation. These investigators observed no consistent relation, either direct or indirect, between the degree of elevation of neutral fat and that of cholesterol in repeated determinations in the same patient.

The lowering of all lipid levels in response to treatment with thyroid and thyroxin, their prompt rise following suspension of treatment (Wilkins and Fleischmann [7]) and the failure of iodine therapy to effect a reduction are apparent from chart 3.

6. Peters, J. P., and Man, E.: J. Clin. Investigation **22**:715, 1943.

6a. Radwin, L. S.; Michelson, J. P.; Melnick, J., and Gottfried, S.: Blood Lipid Partition in Hypothyroidism of Childhood, Am. J. Dis. Child. **60**:1120 (Nov.) 1940.

7. Wilkins, L. W., and Fleischmann, W.: J. Clin. Endocrinol. **1**:1, 14, 91 and 98, 1942.

Hepatic Disease.—Relatively low total cholesterol and decided reduction of cholesterol ester (ratios of ester cholesterol to total cholesterol, 0.37 and 0.28; normal 0.69) were the principal changes observed during the active stage in a patient with subacute catarrhal hepatitis. This change was accompanied with a moderate drop in total lipid. Tests of hepatic function demonstrated damage to the liver. With clinical recovery, the lipid pattern became normal (chart 4, case 15). Hodges, Sperry and Andersen [3a] noted reduction of ester cholesterol in a series of 10 children with acute catarrhal hepatitis.

Cholesterol partition was normal in a patient with congenital biliary stenosis with cirrhosis (case 16).

The adult with xanthomatous biliary cirrhosis (chart 4) presented an unusual example of relative ester cholesterol depression. The ester

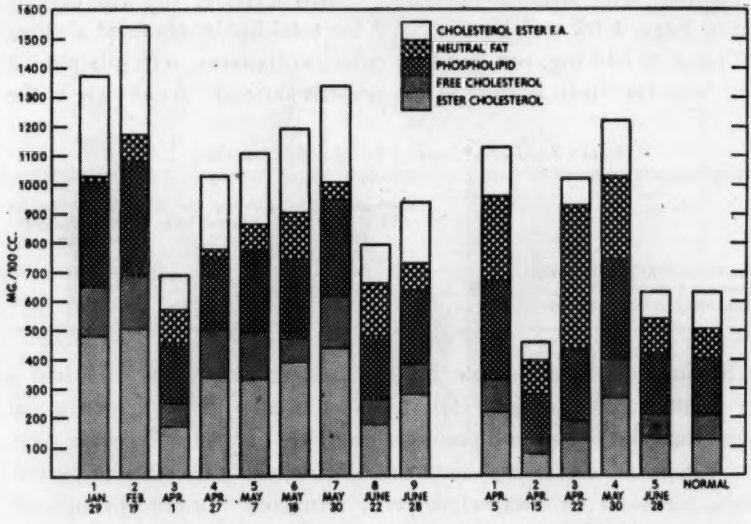

Chart 3.—Variations in lipid levels in 2 patients with cretinism, determinations for which were made under conditions listed in table 4. The first nine determinations were made in case 10, while the second five were made in case 11.

cholesterol of only 180 mg. per hundred cubic centimeters in a total cholesterol of 910 mg. per hundred cubic centimeters makes the ratio of ester to total cholesterol, 0.2. Thannhauser [8] reported similar observations in this disease and attributed the low percentage of ester cholesterol to damage of the liver.

Diabetes Mellitus.—A majority of the 8 diabetic children had high normal to slightly elevated total lipids. In most cases this was accounted for by rises in both the phospholipid and the total cholesterol. Cholesterol

8. Thannhauser, S. J.: Lipidoses in Christian, H. A.: Oxford Loose-Leaf Medicine, New York, Oxford University Press, 1940, vol. 4, chap. 7 A, p. 214.

partition was normal in all but 1 patient (case 20), whose ester cholesterol was reduced (ratio of ester cholesterol to total cholesterol, 0.33).

TABLE 4.—*Data on Two Patients with Cretinism*

	Case 10							
Determination	1	2	3	4	5	6	7	8
Date	Jan. 29	April 1	April 27	May 7	May 18	May 30	June 22	June 28
Medicament								
Thyroid	0	½ grain daily Feb. 21 to March 25	0	0	0	0	0	0
Thyroxin	0	0	0	0	0	0	Single dose, 3 mg. on May 31	0
Other medicaments	0	0	0	Strong iodine solution (U.S.P.), 10 drops daily since April 28	Strong iodine solution (U.S.P.), 10 drops daily	Strong iodine solution (U.S.P.), 10 drops daily	0	0
Clinical state	Severely hypothyroid	Decided improvement	Irritable, sluggish	Same	Same	Slightly less irritable	More alert; less irritable; improved speech	No data

	Case 11				
Determination	1	2	3	4	5
Date	April 5	April 15	April 22	May 30	June 28
Medicament					
Thyroid	0	0	0	0	½ grain daily since May 30
Thyroxin	0	Single dose 3 mg., on April 6	0	Single dose 3 mg., on April 27	0
Other medicaments	0	0	0	0	0
Clinical state	Severely hypothyroid bone age, 1 mo.	Improved; more alert	About the same	More active	Alert; improved mentally

TABLE 5.—*Percentage of Total Lipid Increase*

	Increase Due to Cholesterol (%)	Increase Due to Neutral Fat (%)	Increase Due to Phospholipid (%)
Case 10 (untreated)	90	0	10
Case 11 (untreated)	40	40	20

In none of the 8 diabetic children was the diabetes seriously out of control, though the urine of only 1 child (case 24) was free of sugar at the time of the study.

Such lipid elevations as occurred in this group did not necessarily accompany either high blood sugar levels or treatment with large doses

of insulin (chart 5). It will be recalled that Rabinowitch,[8a] working in 1929, observed a positive correlation between total cholesterol levels and glycosuria, as well as between total cholesterol and required insulin dosage.

Glycogenosis.—Attention is directed to the following changes in the lipid levels in a patient 18 months of age, with glycogenosis (case 26): (1) the excessively high total lipid levels attained, (2) the high level of neutral fat, accounting for most of the total lipid elevation, (3) the relatively moderate rise in values for cholesterol in the first and second

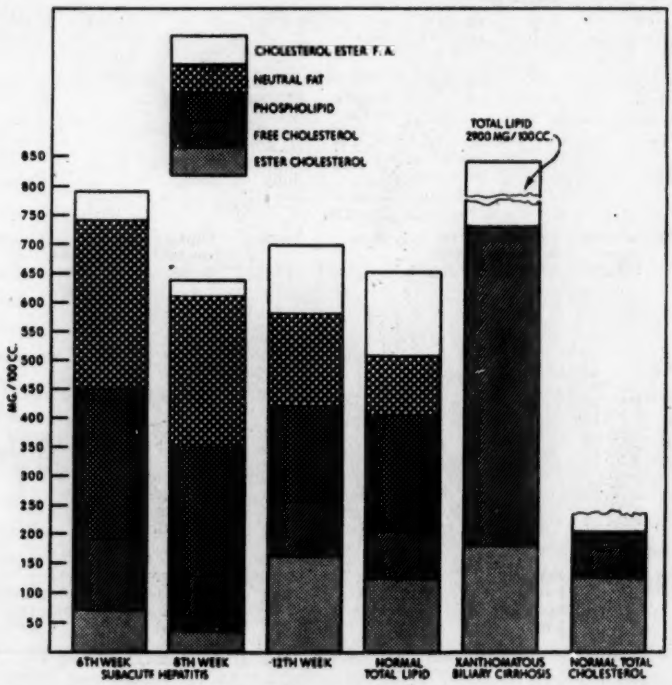

Chart 4.—Variations in lipid patterns of patients with hepatic disease. The first three columns show the values in a child with subacute catarrhal hepatitis (case 15). The fifth column represents the lipid values of an adult with xanthomatous biliary cirrhosis. The fourth and sixth columns indicate normal values.

determinations (*A* and *B*) (chart 6) and its low-normal value in the third determination (*C*) and (4) the reduced ratio of ester to total cholesterol in the first and second determinations.

Two clinical notes are of possible significance for further study: (1) between the first and second determinations the child received lipocaic, and (2) the third determination was made shortly before his death of

8a. Rabinowitch, I. M.: The Cholesterol Content of Blood Plasma in Juvenile Diabetes: A Statistical Study, Arch. Int. Med. **43**:372 (March) 1929.

severe ketosis and acidosis, precipitated by an apparently mild infection of the respiratory tract.

While blood lipid elevation appears to be an inconstant feature of glycogenosis as reported in the literature, high total lipid levels with an excessive neutral fat component, as in this case, are on record.[9]

Nutritional Disturbances.—Moderate undernutrition produced no noteworthy changes in the total lipid, phospholipid or cholesterol levels of 3 patients. An undernourished girl of 10 years (who was also asthmatic) had low total lipid and total cholesterol levels.

Hodges and his associates [3a] reported an average cholesterol level of 123 mg. per hundred cubic centimeters in 78 children with loss of weight due to malnutrition.

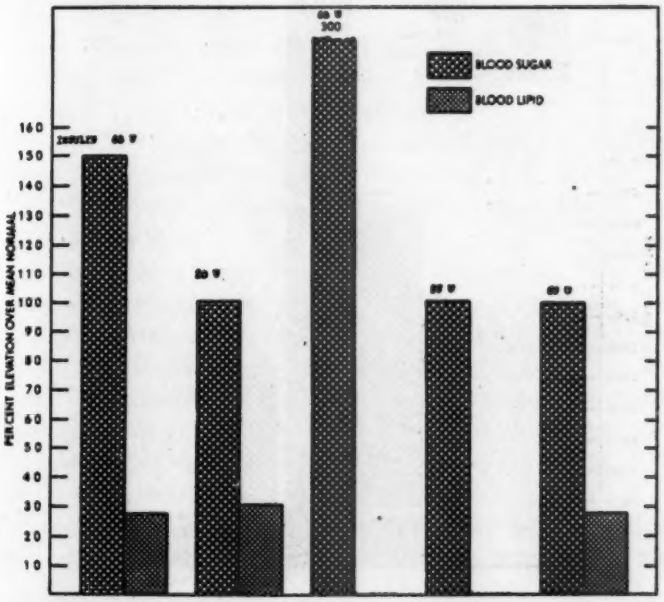

Chart 5.—Blood lipid and blood sugar levels in 8 children with diabetes mellitus (cases 18 to 22).

Uniform reduction of all lipids occurred in a 1 year old boy with congenital pancreatic fibrocystic disease of nine months' duration. A boy of 3 years, with carotenemia, showed a uniform elevation of all lipids. His ester cholesterol to total cholesterol ratio was normal.

Three out of 5 patients with juvenile obesity had normal total lipid levels. In 2 whose total lipid and total cholesterol levels were somewhat elevated, a basal metabolic rate of — 20 suggested hypothyroidism.

9. Hogg. P., and Sidbury, J. B.: J. Pediat. **10**:798, 1937. van Creveld, S.: Medicine **18**:1, 1939.

Investigators have reported the cholesterol levels of obese children without hypothyroidism to be normal.[10]

Rheumatic Fever.—No significant deviations from the normal were observed in the lipid levels of 11 patients with rheumatic fever. The disease was active, or recently active, in 6 of these and quiescent in 5.

Rheumatoid Arthritis.—All lipid levels were reduced in the second patient (case 50). This patient was seriously undernourished. The first patient (case 49), whose lipids (except for phospholipid) were within the normal range, was in better nutritional condition. It is difficult to rule out the role of the nutritional state in the reduction of

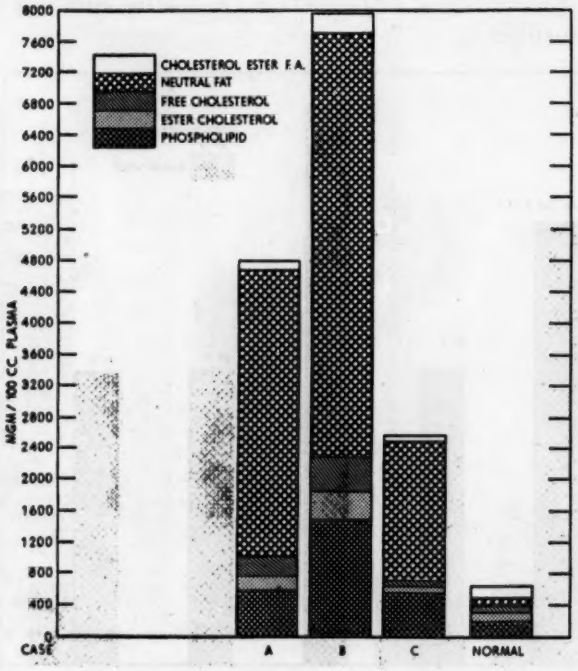

Chart 6.—Changes in lipid levels in a patient with glycogenosis (case 26).

lipids observed in these patients. Normal lipid values have been reported for adults with rheumatoid arthritis.[11]

SUMMARY AND CONCLUSIONS

A study of the total and fractional plasma lipid levels in 50 children with various diseases demonstrated in certain instances levels which were abnormal by comparison with those of 24 normal children.

10. Peters, J. P., and Man, E.: J. Clin. Investigation **22**:707, 1943. Thannhauser.[8]

11. Block, W. D.; Buchanan, O. H., and Freyberg, R. H.: Serum Lipids in Patients with Rheumatoid Arthritis and in Patients with Obstructive Jaundice: A Comparative Study, Arch. Int. Med. **68**:18 (July) 1941.

Since this series is too small to permit conclusions as to the constancy of the observed deviations from the normal, those observations for which confirmation is especially indicated are briefly summarized.

The most seriously abnormal blood lipid levels in the series were encountered in patients with nephrosis, hypothyroidism, glycogenosis and hepatic parenchymal disease. The lipids of patients with partially controlled diabetes mellitus showed some suggestive changes.

In a patient with nephrosis, observed through a major portion of the course of the disease, shifts in the relative proportions of cholesterol and neutral fat accompanied changes in the clinical picture. A preponderance of cholesterol in the early stage was replaced with a decided excess of neutral fat during severe phases, when the total lipid was highest. During convalescence neutral fat returned to normal, but cholesterol remained high.

In the aforementioned patient with nephrosis the ratio of ester cholesterol to total cholesterol appeared to decrease during severe phases and to increase during convalescence.

Of the 2 children with cretinism, 1 showed a higher relative cholesterol level and a lower neutral fat level than did the other. These differences were evident whenever the levels were elevated during three months of obsrvation.

A moderate drop in total lipid levels occurred in 1 patient during the active phase of subacute catarrhal hepatitis. Depression of the level of ester cholesterol, as previously described by Hodges, Sperry and Andersen, was also observed.

Three determinations in a patient with glycogenosis demonstrated high and variable total lipid levels, composed chiefly of neutral fat. Total cholesterol elevation was by comparison moderate. The ratio of ester to total cholesterol was somewhat low.

Uniform moderate increase of all the lipids occurred in a patient with carotenemia. The ratio of ester to total cholesterol remained normal.

5746 Drexel Avenue (37).

INFECTION WITH SALMONELLA TYPHIMURIUM IN THE NEWBORN

Epidemiologic and Clinical Considerations

HAROLD ABRAMSON, M.D.
NEW YORK

IN 1939, an outbreak of infection with Salmonella panama was reported in a group of newborn infants in a hospital nursery.[1] The source of the infection was traced to a nurse who had cared for the babies. In agreement with the observations of Schiff,[2] the severity of the disease and the many complications caused by the panama variety of Salmonella pathogens were stressed. Differentiation of Salmonella infection of the newborn from epidemic diarrhea of the newborn was also considered.[3] In addition, attention was called to the variability in symptomatology, clinical course and complications induced by organisms of the Salmonella group. This problem subsequently was discussed further by Seligmann and Hertz.[4]

The diversity in the clinical picture of Salmonella infections in the newborn again is shown by the three related outbreaks of infection with Salmonella typhimurium now reported. These outbreaks illustrate the importance of making early diagnostic cultures of the feces in all suspected cases of diarrhea, and demonstrate the necessity for recording accurately the case histories of maternity patients directly on admission, particularly with respect to previous gastrointestinal upsets. The need for scrupulous cleanliness in the conduct of maternity services is also shown, with emphasis on such procedures as careful hand scrubbing by

From the Bureau of Preventable Diseases, New York City Department of Health, and the Department of Pediatrics, Beth Israel Hospital, service of Dr. Philip Cohen.

1. Abramson, H.; Frant, S., and Oldenbusch, C.: Salmonella Infection of the Newborn: Its Differentiation from Epidemic Diarrhea and Other Primary Enteric Disorders of the Newborn, M. Clin. North America **23**:591-606 (May) 1939.

2. Schiff, F.: Salmonella Panama: Occurrence of Serious Infections in Infants in New York City, J. A. M. A. **111**:2458-2460 (Dec. 31) 1938.

3. Abramson, H., and Frant, S.: Epidemic Diarrhea of the New-Born: Clinical Considerations, Am. J. Dis. Child. **55**:1288-1307 (June) 1938.

4. Seligmann, E., and Hertz, J. J.: Salmonella Infections: Report on Thirty-Seven Cases Observed at Beth Israel Hospital, New York, in the Past Four Years, Ann. Int. Med. **20**:743-751 (May) 1944.

personnel and patients. Comment will be made on the oral administration of streptomycin in attempts to control infection with S. typhimurium in newborn babies. Observations on the therapeutic effect of streptomycin in these babies were previously reported by Seligmann, Barash and Cohlan.[5] Reference to their results will be made subsequently.

THE OUTBREAKS

Introduction of Infection to the Maternity Floor.—The source of the first outbreak was an infected mother, in circumstances similar to those causing the outbreak reported by Watt and Carlton in a group of premature babies.[6] On March 27, 1946, a mother who had had an intestinal upset four days previously was admitted to the maternity services of the Beth Israel Hospital. The presence of this source case on the obstetric floor soon led to a primary and two recurrent outbreaks of S. typhimurium infection among the mothers and babies. By the time the outbreaks had run their course, 14 babies, and probably 2 others, had become ill among the 120 infants under risk of infection. Of the babies, 11 were clinically ill; the remaining 5 were asymptomatic. The last infant became ill on May 16. In addition, 2 other mothers and 1 intern showed evidence of "silent" infection. The only death was that of the baby of the mother who introduced the infection to the maternity floor.

The Maternity Hospital.—The general hospital in which the outbreaks took place has two floors devoted to lying-in services. Each floor is independently supervised and has its own labor and delivery rooms, formula room and nursing personnel. The same attending obstetric staff serves the two floors. The building is H-shaped and is so arranged that small nurseries serve each wing of the maternity floors. These floors consist of single bedrooms, and every two rooms are connected by a common utility room, containing a bedpan flusher but no sterilizer. The outbreaks were confined to one floor only. With these salient features in mind, a study of the sequence of events in the outbreaks is next in order, with the causative organism S. typhimurium used as the tracer. The bacteriologic studies in these outbreaks were made under the direction of Dr. Erich Seligmann.

The Clinical Picture.—It will be recalled that in infection of the newborn with S. panama the clinical picture is that of severe sepsis with localization of the infection in the meninges, peritoneum and pleura.[1]

---

5. Seligmann, E.; Barash, L., and Cohlan, S. Q.: Streptomycin Treatment of Salmonella Enteritis in Infants, J. Pediat. **30**:182-189 (Feb.) 1947.

6. Watt, J., and Carlton, E.: Studies of the Acute Diarrheal Diseases: XVI. An Outbreak of Salmonella Typhimurium Infection Among Premature Infants, Pub. Health Rep. **60**:743-740 (June 29) 1945.

Bronchopneumonia and otitis media may also occur. By contrast, the clinical course of infection with S. typhimurium is much milder and is strikingly similar in all cases. With the exception of the baby who died, none of the infants with the disease appeared unusually ill. As will be seen from the case histories, the onset was acute and took place on the second postnatal day in 7 of the 11 sick babies. Illness was ushered in by an abrupt rise in temperature from 101 to 104 F. Stools became more frequent and were of loose, green, mucoid character; no blood was seen. The stools were not the yellowish and watery evacuations typical of epidemic diarrhea of the newborn.[3] Dehydration and loss of weight were not great, and there were no complications. Because of the age of the infants, blood counts were not of diagnostic value. Except for the single fatality, the infants responded well to treatment. The duration of illness averaged two weeks.

FIRST OUTBREAK

The first outbreak involved the mothers in rooms 505, 507 and 508, southwest wing, and the babies in the southwest and northwest nurseries.

Initial, or Index, Case.—The first case occurred in southwest nursery 1.

CASE 1.—Baby S., a white girl, was born normally on March 27, at full term, weighing 3,202 Gm. On the first day abdominal distention was present, and on the second day green stools were noted. The temperature rose to 101 F., and the weight dropped to 2,977 Gm. On the third day the baby became very ill; abdominal distention increased, and a slight redness, but no swelling or edema, was seen about the umbilicus. On the fourth day the infant weighed 2,778 Gm. and had frequent, green stools. A few moist rales were heard at the base of the left lung. Penicillin therapy was begun. That night considerable vomiting occurred. The picture suggested possible intestinal obstruction, and a scout plate of the abdomen was taken. Nothing of significance was noted. A diagnosis of primary enteric infection was then made, and succinylsulfathiazole ("sulfasuxidine") was substituted for the penicillin. Fluids were given intravenously. On April 1, the fifth postnatal day, culture of the stool yielded S. typhimurium. The baby died on April 2, at the age of 6 days, weighing 2,765 Gm.

Postmortem examination, by Dr. Henry Brody, showed severe ulcerative enteritis, involving mainly the cecum, and extensive aspiration pneumonia. In the opinion of the pathologist, the latter was the primary cause of death. From the mother's history (case 2, Mrs. S.), the possibility was also suggested that the infection may have arisen in intrauterine life and was virulent enough to cause the baby's death.

The Source Case.—With the cause of the baby's illness now known, reference was made to the mother as the probable source of the infection.

CASE 2.—On March 27, Mrs. M. S., aged 28, was admitted to the maternity services and gave birth to her baby (case 1, newborn infant S.). The record of the case history showed nothing regarding the patient's health prior to admission to the hospital. After her delivery the mother was placed in room 508, where

she remained until March 31. She was then transferred to room 507, directly across the corridor. This room is connected with room 505 by a common utility room (case 4, Mrs. O.). Mrs. S. was moved in her bed to room 507, but her bedpan, not sterilized terminally, was left in the utility section of room 508. When the nature of the illness of her baby was established, a sample of stool from Mrs. S. was cultured. This culture yielded S. typhimurium on April 3. Close questioning of Mrs. S. now revealed that on March 23, four days prior to her admission to the hospital, she had been ill with vomiting and diarrhea. No other member of the household was similarly affected. The mother was immediately removed from the maternity floor and placed in isolation; she was discharged from the hospital on April 7.

Spread of Infection Among Mothers in Southwest Wing.—The mothers in rooms 505, 507 and 508 were studied.

CASE 3.—Immediately after Mrs. S. (case 2) had been moved, on March 31, to room 507, Mrs. D. was admitted into her place in room 508. Mrs. D., aged 33, had been delivered of a normal infant on March 31. Although she was asymptomatic, culture of feces yielded S. typhimurium on April 4. Since Mrs. D. used the unsterilized bedpan previously used by Mrs. S., soiling of the hands evidently took place. With inadequate hand scrubbing, there was gross contamination of food subsequently ingested. The stools of this mother's baby were negative for enteric pathogens. Mrs. D. was immediately isolated and was discharged to her home on April 13.

CASE 4.—In a similar manner, Mrs. S. (case 2) was also responsible for the spread of the infection to Mrs. O., aged 29, who was admitted on April 3 to room 505, directly connected with room 507 by a common utility room. Mrs. O. was delivered of a normal baby on April 3, and on April 5 fever (temperature, 100.2 F.) developed. She was given sulfadiazine therapy. There was no history of diarrhea. On April 6 a fecal culture yielded S. typhimurium. A culture of the baby's stool showed no growth of enteric pathogens. Here, too, improper handling of bedpans in the common utility room and gross soiling of hands and of food probably accounted for the spread of the infection from Mrs. S. to Mrs. O. On April 7 this mother was discharged with her baby.

Spread of Infection Among Babies in Southwest Nursery 1.—After exposure of the babies in southwest nursery 1 to the infection of infant S. (case 1), evidence of spread was revealed by the presence of S. typhimurium in the fecal cultures of 2 asymptomatic babies.

CASE 5.—Baby Fr., a white girl, was born on March 26, at full term, weighing 2,778 Gm. The baby was placed in the southwest nursery and appeared well until her discharge from the hospital, on April 4, weighing 2,805 Gm. A culture of the stool yielded S. typhimurium on April 4. Culture of the mother's stool was negative for pathogens.

CASE 6.—Baby L., a white boy, born at full term on March 26, was also placed in southwest nursery 1. The weight at birth was 3,090 Gm. Postnatal progress was good, and the baby was discharged home on April 4, at the age of 9 days, weighing 2,977 Gm. On April 4 a culture of the feces showed S. typhimurium. The mother's stools showed no growth of enteric pathogens.

Spread of Infection to Babies in Northwest Nursery 2.—An effort was made to keep the infection within the southwest wing of the

maternity floor by closing this section to further admissions on April 3. Because of the shortage of nursing personnel, it was not possible to make the separation complete, since the nurses could not be confined to duty in the contaminated wing. As a result, spread of the infection soon became apparent in northwest nursery 2, where 2 babies became acutely ill. As the infection spread from one wing to another, various sections of the maternity floor were shut off until the entire service was closed, on April 4.

CASE 7.—Baby Fi., a white girl, was born normally on March 31, weighing 3,969 Gm. Her progress was favorable until April 2, when the temperature rose to 104 F.; it continued to be high throughout the next day. The stools were normal. Supportive therapy was given. A specimen of stool cultured on April 3 yielded S. typhimurium. The mother's stool was negative for enteric pathogens. On April 4, when the baby was 4 days of age, the temperature fell to 99 F., and on the next day the stools increased in frequency and were loose and green. Succinylsulfathiazole was given. No difficulty was encountered in correcting the diarrhea, and the infant was discharged on April 18, in good condition, at the age of 18 days, weighing 3,912 Gm. Culture of a stool obtained on April 12 yielded no organisms.

CASE 8.—Baby B. was born normally on April 1, at full term, weighing 3,713 Gm. On April 3, at the age of 2 days, the baby's temperature rose to 102 F., and then to 103 F. on the following day. The stools increased in frequency and were green and mucoid. Culture of a stool on April 4 yielded a growth of S. typhimurium. The mother's stools showed no enteric pathogens. The temperature soon leveled off, and the stools became normal. The baby was discharged on April 18, at the age of 17 days, weighing 3,657 Gm. Culture of a stool on April 16 still yielded S. typhimurium.

Spread of Infection to the Intern Staff.—Fecal cultures from the personnel of the maternity service revealed that a member of the obstetric intern staff had stools positive for the organism.

CASE 9.—Coming to Beth Israel Hospital as an affiliate intern in obstetrics, Dr. W. was assigned on April 2 to service in the northwest nursery, where he examined and gave clyses to baby Fi. (case 7). Rubber gloves were not worn while he was handling the baby. On April 3 Dr. W. also attended without gloves and gave clyses to baby B. (case 8). In all likelihood, sufficient soiling of the hands occurred to cause contamination of food subsequently ingested, for on April 4 samples of feces from this intern yielded the organism. There was no overt clinical sign or symptom. The intern was immediately removed from duty. There was no previous history of an intestinal upset.

Possible means by which the infection may have spread from southwest nursery 1 to northwest nursery 2 were sought. Consideration was given to the formulas as a possible vehicle of infection. However, if gross contamination of the formulas had taken place the outbreak would have been of the explosive type, with simultaneous appearance of infection in many babies in all the nurseries. Secondary carriers were sought among the nurses on relief duty, the regular nursing personnel, the interns and the attending physicians, but none was

suspected, either clinically or as the result of fecal cultures. Moreover, the same attending medical staff served the fourth floor obstetric service, where no instance of diarrhea occurred among either the babies or the mothers. The only possible source of infection responsible for the spread was a nurse who was assigned to duty in all branches of the maternity and newborn nursery services. After relief duty in southwest nursery 1, with exposure to baby S. (case 1), who became ill in March 27, the nurse became acutely ill with vomiting and diarrhea on March 31. On the following day, April 1, she was assigned to duty in northwest nursery 2. Baby Fi (case 7) and baby B. (case 8) became ill on April 2 and 3, respectively. It is likely that the infection was carried from one nursery to another through this nurse. However, cultures of her stools yielded no enteric pathogens, and the impression could not be substantiated.

SECOND OUTBREAK

The second outbreak involved the babies in northwest nursery 2. Services on the maternity floor were resumed on April 9. It was thought that the infection had been cleared from the floor, and there was great surprise when, on April 15, cultures of stools yielding S. typhimurium were obtained from 2 babies in the northwest nursery. As a precautionary measure, services were again closed on April 15, and the floor was cleared of patients.

CASE 10.—Baby Fo., a white boy, was born normally on April 13, weighing 3,147 Gm. On April 15 the temperature rose to 101 F., with a later rise to 103 F. Frequent brownish stools, containing no blood or mucus, developed. The baby was isolated. Culture of a stool on April 15 showed growth of S. typhimurium. A second culture, on April 19, also yielded the organism, but one made on April 22 showed no growth. The baby was discharged well on April 26, at the age of 13 days, weighing 3,232 Gm. Cultures of stools from the mother were negative for the organism.

CASE 11.—Baby He., a boy, was born by uncomplicated delivery on April 10, at full term, weighing 3,884 Gm. He thrived normally and was asymptomatic throughout his stay in the hospital. On April 18, at the age of 8 days, and weighing 4,054 Gm., the baby was discharged from the hospital. Culture of a stool on April 15 yielded S. typhimurium. Culture of the mother's stools did not yield the organism.

Once again the stools from all personnel of the maternity service and from all other persons on the maternity floor were cultured to determine the existence of any secondary carrier. No enteric pathogens were recovered from this sampling; nor did cultures of the stools of the mothers yield the organism. This investigation gave no clue to the origin of the positive cultures from the 2 babies. Therefore, after terminal sterilization of equipment and reexamination of the personnel, the maternity services were reopened, on April 21.

THIRD OUTBREAK

The third outbreak involved the babies in southwest nursery 1 and northwest nursery 2. Attempts were made to control the infection with oral administration of streptomycin.

Southwest Nursery 1.—Three weeks elapsed and the situation appeared favorable, when, on May 14, further evidence of S. typhimurium infection appeared among the babies in the nurseries of the fifth floor maternity service. In this recurrent outbreak, cultures of the stools of 5 babies in the southwest nursery yielded the pathogen. A search of the records of the babies discharged from the hospital during May disclosed 2 others with possible infections, but no cultures had been made of the stools of these babies. In addition, 2 babies in northwest nursery became acutely ill and cultures of their stools yielded S. typhimurium. Thus, this outbreak involved 7 babies, and possibly 2 more, among 60 infants under risk of infection. It was now possible to observe the effect of oral administration of streptomycin in controlling infection with S. typhimurium among newborn infants. The study by Seligmann, Barash and Cohlan [5] to determine the therapeutic value of streptomycin was in progress at this time.

CASE 12.—On May 14, at the age of 2 days, Baby Kl., a white boy, born at full term and weighing 3,912 Gm., had a rise in temperature to 102 F. and loose, green stools. The next day the temperature was 104 F. and on the following day 101 F. Culture of the stools taken on May 16 yielded S. typhimurium. The temperature was normal the next day, but the stools continued to number from six to eight a day. Culture of the stool again yielded the organism on May 21. Streptomycin therapy was begun on this day, in an oral dosage of 200 mg. a day. From May 21 to May 24 a total of 600 mg. was given. Culture of the stool on May 23 showed "no growth," but cultures on May 27, 28, 29 and 30 and on June 1 again yielded S. typhimurium. Streptomycin again was given orally on June 1 and June 2 with a total dose of 1,600 mg., and once again cultures of the stool yielded "no growth" of organisms. The baby was discharged from the hospital on June 3, aged 22 days, in good condition. The stools were normal. A follow-up culture of the stool made on June 10, yielded S. typhimurium.

CASE 13.—On May 15, two days after birth, baby Ho., a white boy, born at full term, with a weight of 3,317 Gm., had a temperature of 101 to 103 F. and frequent loose stools. Culture of the stool on this day yielded S. typhimurium. The temperature was normal the next day, but the diarrhea continued. On May 21 streptomycin therapy was begun, in an oral dosage of 200 mg. a day. This therapy was continued until May 23, a total dose of 600 mg. being given. The stools yielded S. typhimurium on May 22 but showed "no growth" on May 23 and 24. Cultures yielding the organism were obtained on May 25 and 27. On May 29 and 30 a total dose of 1,200 mg. of streptomycin was again given, and culture of the stools on May 29 and 30, even on enriched mediums, showed "no growth" of organisms. The baby was discharged from the hospital on June 3, aged 19 days, in good condition. Follow-up cultures of the stools taken on June 7 and 10 again yielded growths of S. typhimurium, a result similar to that recorded for baby Kl. (case 12).

CASE 14.—Born on May 17, baby E., a white girl, weighing 3,713 Gm., became ill, with loose green stools, on May 19. On May 20, when her temperature was 101 F., culture of a stool yielded S. typhimurium. From May 20 to May 24 a total dose of 1,200 mg. of streptomycin was given orally. Repeated cultures of the stool on May 22, 23 and 24 showed "no growth." Cultures of stools taken on May 28, 29 and 30 and on June 1 again yielded a growth of the organism. From June 1 to 4 administration of streptomycin was repeated, 1,200 mg. being given orally and 600 mg. intramuscularly, for a total dose of 1,800 mg. Cultures of stools showed "no growth" on June 4 and 5 but again yielded organisms on June 9, 10 and 11, after cessation of treatment. Trouble was experienced in controlling the diarrhea of this baby. The carbon dioxide-combining power of the blood was depressed to 20 volumes per cent. Intravenous therapy checked the condition, however, and an uneventful recovery was made. The baby was discharged on June 28 at the age of 42 days.

CASE 15.—This asymptomatic case of infection with S. typhimurium was discovered by means of culture on May 20. Baby Ro., a white boy, born at full term, with a weight of 2,720 Gm., was discharged home in good condition on May 20, before the result of culture of the stool was known. On the last follow-up report the baby was doing well.

CASE 16.—Baby Di., a white boy, born at full term, with a weight of 3,458 Gm., was asymptomatic throughout his stay in the hospital. On the day of his discharge, when he was 6 days of age and weighed 3,372 Gm., a culture of the stool yielded S. typhimurium.

The onset of the outbreak in southwest nursery 1 may have had its beginning somewhat earlier than May 14 (case 12, baby Kl.). Search of the records of the babies discharged from the hospital just prior to recognition of the initial case disclosed 2 possible instances of the disorder. No culture of the stool was made for either baby, but the histories are given because of their similarity to the proved cases of infection.

CASE 17.—Baby T., a white boy, born on May 3, with a weight of 3,685 Gm., had loose stools and a temperature of 103 F. on the second day. The temperature continued at 102 F. on the third day and reached 101 F. on the fourth day. The stools were green and loose. The baby was discharged home on May 13, at the age of 10 days, weighing 3,372 Gm.

CASE 18.—Baby Bog., a white boy, was born on May 1, at full term, weighing 2,523 Gm. On May 6 loose stools appeared and vomiting developed; the temperature was 100 F. The next day the temperature rose to 103 F. and the loose stools continued. The baby made an uneventful recovery and was discharged home on May 9, at the age of 8 days, weighing 2,500 Gm.

Northwest Nursery 2.—First knowledge of the reappearance of infection in northwest nursery 2 was had on May 17 from the report that S. typhimurium had been cultured from the stool of a 6 day old baby.

CASE 19.—Baby Kr., a white boy, was born on May 11, at full term, weighing 3,911 Gm. On the second day the temperature rose to 102 F. in the evening. This rise continued to 103 F. on the third day, and the temperature varied between 101 and 102 F. during the next two days, with eight to nine green mucoid stools

daily. On May 17 a fecal culture yielded S. typhimurium. The temperature became normal on the sixth day. Cultures of stools on May 21, 24 and 25 still yielded the organism. From May 27 to 29 a total dose of 1,200 mg. of streptomycin was given orally. On May 28, 29 and 30, specimens of the stool cultured on enriched mediums yielded "no growth." On May 31 and June 1 and 3, after cessation of treatment, the stools again yielded the pathogen. The baby was discharged on June 3, at the age of 23 days, in good condition. Follow-up cultures of the stools on June 5, 8 and 10 showed persistence of the organisms.

CASE 20.—Born at full term on May 14, weighing 3,572 Gm., baby P., a white girl, became ill with fever (temperature, 102 F.) and loose stools on the second day. The temperature continued to be elevated into the third day, May 17, when a culture of the stool yielded S. typhimurium. Additional cultures positive for the organism were obtained on May 21, 24, 27, 29 and 30 and on June 1. From June 1 to 4, 1,600 mg. of streptomycin was given orally. Cultures of the stool showed "no growth" of organisms during that period. With cessation of streptomycin therapy, however, cultures again yielded the pathogen on June 5, 8 and 10. The baby was discharged from the hospital on June 6, at the age of 23 days, in good general condition.

Again, fecal cultures were taken from the maternity patients and the medical and nursing personnel, but the carrier responsible could not be identified. Further search proved futile.

VALUE OF STREPTOMYCIN IN CONTROL OF INFECTION

Because of the few cases and the limited amount of streptomycin available, only impressions of the effect of the drug on infection with S. typhimurium can be given; no conclusion can be drawn. As was stated previously, the results of treatment with streptomycin of S. typhimurium infection in 5 newborn babies were recently reported by Seligmann, Barash and Cohlan.[5] These investigators observed that oral administration of streptomycin did not appear to alter either the clinical course or the duration of the disease in the 5 newborn infants studied, as compared with the babies who did not receive the antibiotic substance. They also noted that the effect of streptomycin on the Salmonella organisms is bacteriostatic, an observation supported by animal experimentation.[7]

In this connection, the effect of streptomycin on the bacterial flora of the intestinal tract, as determined by fecal cultures, is of importance from the point of view of public health. It has been shown in the case histories that while the infants were given streptomycin orally for three to four days in doses of from 25 to 100 mg. every three hours for eight doses, cultures of stools were obtained showing "no growth" even on "enriched mediums." However, within one to three days after cessation

7. Seligmann, E., and Wasserman, M.: Studies on Streptomycin in the Salmonella Field, read before the New York Board of American Bacteriologists, Oct. 22, 1946.

of therapy fecal cultures yielding the organism were again obtained from all 5 infants. This suppression, not only of the pathogenic organism but of the normal bacterial growth in the intestinal tract as well, was demonstrated again in 3 of the 5 infants. On cessation of treatment the organisms were once again grown in fecal cultures.

Since the babies were kept in the same nursery during and after treatment, recontamination from baby to baby may possibly have occurred. The results would, no doubt, have been more reliable had it been possible to care for each baby in a separate room. Furthermore, the duration of treatment and the oral dose employed may have been insufficient to clear permanently the S. typhimurmium from the stools of the babies.

This experience is similar, however, to that with administration of sulfonamide compounds in treatment of Shigella infections. It has been frequently observed at the Department of Health that the sulfonamide drugs induce complete suppression of growth of organisms in the intestinal tract. But unless medication is of sufficient duration, depending on clinical indications, and of adequate dosage, fecal cultures yielding growths will be obtained within two to three days after therapy is suspended. In fact, the department of health has adopted the procedure of accepting stools for terminal culture only after the lapse of two or three days after the patient's release from sulfonamide treatment. The same precaution appears to be indicated in termination of cases with streptomycin. It should be noted that the recent reports of the National Research Council [8] on streptomycin therapy as applied to Salmonella infections also showed disappointing results. The Council recommended that treatment of these infections be continued at least two weeks and that it be started early. The intramuscular route of administration is the method of choice.

In passing, attention is called to the necessity of supplementing with adequate rations of vitamins, notably the vitamin B complex and vitamin K, the diets of infants receiving either streptomycin or the sulfonamide compounds for diarrheal disorders or other infections. As has been shown by Cowgill [9] and by Rapoport and Dodd,[10] the suppressive action of streptomycin and of the sulfonamide drugs on the bacterial flora ordinarily synthesizing the vitamins causes rapid depletion of the limited stores of these vitamins in the infants under treatment, thus hampering their recovery from illness.

---

8. Keefer, C. S.: Streptomycin in the Treatment of Infections, J. A. M. A. **132**:4-10 (Sept. 7); 70-77 (Sept. 14) 1946.

9. Cowgill, G. R.: The Physiology of Vitamin B_1 in The Vitamins: A Symposium, Chicago, American Medical Association, 1939, chap. 8, pp. 159-178.

10. Rapoport, S., and Dodd, K.: Hypothrombinemia in Infants with Diarrhea, Am. J. Dis. Child. **71**:611-617 (June) 1946.

SUMMARY

Three related outbreaks of infection with S. typhimurium in the newborn are reported in order further to illustrate the considerable variation in the clinical picture caused by the Salmonella group of enteric pathogens. Attention is also called to the importance of making early diagnostic cultures of stools in all cases of suspected or definite diarrhea, and to the necessity of obtaining accurate case histories of mothers admitted to maternity services, particularly with respect to the existence of infection and the occurrence of intestinal upsets. Newborn infants are highly susceptible to infection with Salmonella organisms, and the introduction of these enteric pathogens into a nursery always represents a potent threat to the babies. Also considered is the influence of oral administration of streptomycin on the bacterial flora of babies infected with S. typhimurium from the point of view of termination of cases and the prevention of spread of the infection.

8 East Eighty-Third Street.

DIABETES MELLITUS IN INFANTS UNDER ONE YEAR OF AGE

Report of a Case and Review of the Literature

JOSEPH SCHWARTZMAN, M.D.

MARGARET E. CRUSIUS, M.D.

AND

DONALD P. BEIRNE, M.D.

NEW YORK

DIABETES as a pediatric entity is not uncommon, since it has been found that 5[1] to 5.7 per cent[2] of all persons with diabetes have the onset of their disease during the first decade of life. However, its incidence decreases directly with the decrease in the age period studied. Of a group of 750 patients with juvenile diabetes studied by White,[3] 16 per cent were found to have had the onset before the age of 4 years, whereas the disease occurred before the age of 1 year in only 0.5 per cent. A similar proportion (7 out of 1,430 diabetic children) was noted in her later figures.[2]

In view of the relative rarity of the disease in children under 1 year of age, it would appear important that every new case discovered be reported in order to augment the general knowledge of this group.

With this consideration in view, it was deemed advisable to report a case of the disease which was detected when the child was 7 months of age, and to give also a general review of the literature.

REPORT OF CASE

H. W., a white girl, was born July 25, 1945, at Metropolitan Hospital. Her delivery was normal, labor lasting one hour. The weight at birth was 7 pounds 8½ ounces (3,416 Gm.). Her stay in the hospital was uneventful, and she was discharged on the seventh postnatal day, weighing 7 pounds (3,135 Gm.).

In February 1946, she was treated for bronchopneumonia at City Hospital and recovered in two weeks. On March 8, she was admited to Metropolitan Hospital

From the Department of Pediatrics, New York Medical College, Flower and Fifth Avenue Hospitals and the Metropolitan Hospital, New York.

1. Boyd, J. D., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1946, vol. 3, chap. 12, pp. 1-30.

2. Joslin, E. P.; Root, H. F.; White, P., and Marble, A.: Treatment of Diabetes Mellitus, ed. 7, Philadelphia, Lea & Febiger, 1940, pp. 42, 48, 687 and 692.

3. White, P.: Diabetes in Childhood and Adolescence, Philadelphia, Lea & Febiger, 1932.

for acute bronchitis and was discharged as cured on the twentieth of the same month. During both admissions, no specimens of urine were obtainable for examination.

On March 26, at the age of 8 months, she was readmitted to Metropolitan Hospital with a history of having had a temperature of 104 F. on the previous day. She weighed 15½ pounds (7,030 Gm.). Physical examination revealed rales throughout both lungs, and a diagnosis of acute bronchitis was made. Examination of the blood revealed a hemoglobin content of 10.9 Gm. per hundred cubic centimeters (68 per cent); 3,950,000 red cells and 25,000 white cells, with 50 per cent polymorphonuclear leukocytes (3 per cent immature forms), 49 per cent lymphocytes and 1 per cent mononuclear cells. Routine urinalysis disclosed glycosuria and acetonuria. The blood sugar was found to be 600 mg. per hundred cubic centimeters. Three hours later it was 550 mg. per hundred cubic centimeters. Twenty units of insulin injection U.S.P. was given, after which the infant showed evidence of hypoglycemia but quickly responded to the administration of orange juice.

Repeated urinalyses and determinations of the blood sugar corroborated the early findings. Tests to determine the type of sugar being excreted in the urine showed it to be a fermentable type, later proved to be glucose. Several dextrose tolerance tests were done, and diabetic characteristics were consistently noted in the curve. A similar tendency was detected in one of the two levulose tolerance tests made.

Tests of hepatic function made on two separate occasions at an interval of two weeks failed to reveal any deviation from normal. The serum amylase was slightly elevated during two episodes of infection, but returned to normal when these cleared. Roentgenograms of the skull, chest (on two occasions), abdomen, extremities (for extent of calcification) and wrists (for bone age) showed that all were normal.

During this period, on April 22, a fluctuant abscess developed, which was incised and drained. Penicillin, 10,000 units, was given the patient every three hours, and in ten days the abscess had cleared completely. During this illness the patient's temperature was elevated, diarrhea developed and there was loss of weight of 2½ pounds (1,134 Gm.).

While the patient was in the hospital, except for the one dose, no insulin was given. She was kept on an adjuvant diet conforming to her age and weight, and, beginning on April 27, the following treatment was instituted: thiamine hydrochloride, 30 mg., injected daily intramuscularly; and nicotinic acid, 100 mg.; riboflavin, 10 mg.; pyridoxine hydrochloride, 5 mg., and ascorbic acid, 100 mg. given orally.

Except for the period of the abscess, the patient ate well and gained weight, and her tolerance for sugar increased, as evidenced by reports of urinalyses and individual blood studies. She was discharged on June 11, weighing 15½ pounds (7,031 Gm.).

One week and four weeks after her discharge, the patient was again examined. Her dextrose tolerance curves still revealed a diabetic tendency. The results of an Exton-Rose dextrose tolerance test made on July 22 were in agreement with previous findings. An ophthalmologic examination at this time showed no changes in the fundus.

About one month after her last examination, the infant was readmitted, on August 26, with a temperature of 103 F., and evidence of acute pharyngitis and gingivitis. The hemoglobin content was 8.5 Gm. per hundred cubic centimeters (58 per cent); the red blood cell count, 4,000,000, and the white blood cell count, 8,000, with 22 per cent polymorphonuclear leukocytes (5 per cent immature forms),

73 per cent lymphocytes, 2 per cent eosinophils, and 3 per cent mononuclear cells. The sedimentation rate (Westergren method) was 30 mm. for the hour; the cephalin flocculation test gave a 2 plus reaction; the total cholesterol and cholesterol esters were decreased, and the dextrose tolerance had decidedly decreased. She was treated with penicillin. Ten thousand units was given intramuscularly as an initial dose, and 5,000 units was administered intramuscularly every three hours for five days. After one week, the acute infection had subsided, and hepatic function determined on September 9, was normal, as was the sedimentation rate. Another dextrose tolerance test, on September 17, still showed a definitely decreased tolerance for sugar. The patient was discharged on October 3, having gained 1½ pounds (680 Gm.) while in the hospital.

It is notable that during the periods of infection the diabetic condition was aggravated, and that during normal periods the urine and the fasting blood sugar levels tended to approach normal, although the tolerance curves still demonstrated the diabetic status.

TABLE 1.—*Data on Individual Determinations of the Blood Sugar and Urinalyses*

Date (1946)	Blood Sugar, Mg./100 Cc.	Glycosuria	Acetone
3/27 4 p.m.	600	3+	4+
7 p.m.	550	4+	—
11 p.m. (after administration of 20 units of insulin)	85	2+	—
3/28 9 a.m.	142	1+	—
3 p.m.	115	—	—
9 p.m.	333	3+	—
3/29	130	2+	—
3/30 to 4/ 1	135	1+	—
4/ 6 to 4/10	92	1+	+
4/14 to 4/16	100	1+	—
4/18 to 4/19	92	—	—
4/23 to 4/25	160	1+	—
5/ 8 to 5/15	100	—	—
5/22 to 6/ 3	85	—	—
6/ 6 to 6/18	...	1+	—
6/19 to 6/20	...	—	—
7/17 to 7/18	...	1+	—
8/26 to 9/ 5	...	1+	—
9/21 to 9/27	240	3+	—

Dextrose tolerance tests on the parents and on 6 other children in the family gave normal results; yet the family history revealed that a maternal aunt and cousin had diabetes.

In view of the probability that the trait was hereditary, together with the glycosuria, the diabetic dextrose tolerance curves and the exacerbations during infection, it was felt that this child had true diabetes mellitus.

The laboratory data are listed in tables 1, 2 and 3.

GENERAL CONSIDERATIONS

The earliest detailed report on infantile diabetes was made in 1789 by Rollo,[4] and the first authentic report for infants under 1 year of age was made in 1850.[5] Since then, Knox,[6] Lawrence and McCance,[7]

4. Rollo, cited by Magnano, P.: Osp. maggiore **19**:107, 1931.

5. Limper, M. A., and Miller, A. J.: Diabetes Mellitus with Extensive Gangrene in Early Infancy, Am. J. Dis. Child. **50**:1216 (Nov.) 1935.

6. Knox, J. H. M.: Bull. Johns Hopkins Hosp. **24**:274, 1913.

7. Lawrence, R. D., and McCance, R. A.: Arch. Dis. Childhood **6**:343, 1931.

TABLE 2.—*Results of Dextrose Tolerance Tests*

Date	Amount of Sugar Given, Gm./Kg.	Blood Sugar Values, Mg./100 Cc. Fasting	½ Hour	1 Hour	2 Hours	3 Hours	5 Min. After Administration of Epinephrine
		Patient					
4/ 2	2	214	214	...	238	168	193
4/ 4	2	160	...	240	250	170	230
4/25	1.75	100	...	135	160	205	240
5/ 6	1.75	115	195	200	150	140	
6/27	1.75	88	115	198	232	201	
7/ 3	1.75	103	105	109	104	119	
7/19	1.75	147	252	298	216	120	
7/22	Exton-Rose test 1.75	117	204	188	...	...	
8/28	Exton-Rose test 1.75	270	400	425	475	475	
9/ 4	Exton-Rose test 1.75	185	350	375	375	360	
9/17	Exton-Rose test 1.75	280	400	430	400	230	
5/23	Levulose 1.75	75	94	135	150	115	
6/ 3	Levulose 1.75	120	170	240	200	127	
		Members of Family					
Name	Relationship						
A.	Father	80	130	62	85	80	
M.	Mother	90	95	125	100	70	
M.	Daughter	94	108	125	75	87	
B.	Daughter	94	120	90	94	105	
G.	Daughter	140	125	105	110	90	
G.	Son	...	97	...	80	95	
A.	Son	82	...	100	110	88	
E.	Son	106	110	115	120	106	

TABLE 3.—*Other Laboratory Data* *

	Date 3/28	3/29	3/30	4/10	4/14	4/19	4/24	4/29	6/6	8/26	8/30	9/3	9/4	9/9	9/17
Nonprotein nitrogen, mg.	..	24	29	..	..	..	..	..	..	..	..	..	..	..	..
Urea nitrogen, mg.	..	..	13.5	..	..	..	..	..	..	..	..	..	..	..	..
Creatinine, mg.	..	..	1.2	..	..	..	..	..	..	..	..	..	..	..	..
Icteric index	..	..	5	..	4	..	..	..	..	..	4	..	..	5	..
van den Bergh reaction	..	..	—	..	—	..	..	..	..	..	—	..	..	—	..
Cephalin flocculation	..	..	—	..	—	..	..	..	..	..	2+	..	..	—	..
Phosphorus, mg.	..	..	4.7	..	4.0	..	..	..	..	..	3.5	..	..	4.4	..
Phosphatase, units	..	..	6.5	..	4.4	..	..	..	..	..	6.4	..	..	10.9	..
Total cholesterol, mg.	..	..	210	..	156	..	..	..	..	..	108	..	..	210	..
Free	..	..	60	..	37	..	..	..	..	..	54	..	..	40	..
Esters	..	..	150	..	119	..	..	..	..	..	54	..	..	170	..
Total serum protein, Gm.	..	..	7.2	..	7.2	..	..	..	..	..	7.3	..	..	6.9	..
Albumin, Gm.	..	..	5.0	..	4.7	..	..	..	..	..	4.3	..	..	4.8	..
Globulin, Gm.	..	..	2.2	..	2.5	..	..	..	..	..	3.0	..	..	2.1	..
A/G ratio	..	..	2.2	..	1.9	..	..	..	..	..	1.4	..	..	2.3	..
Serum amylase, units	..	..	..	32	..	..	24	..	..	..	24	..	..	48	16
Serum sodium, mg.	..	..	..	..	..	..	..	..	330	..	..	..	..	..	..
Serum potassium, mg.	..	..	..	..	..	..	..	..	18	..	..	..	..	..	..
Serum chloride, mg.	..	..	..	..	..	..	..	..	621	..	..	..	..	..	..
Wassermann reaction	..	..	—	..	..	..	..	..	..	..	..	..	..	..	..
Kahn reaction	..	..	—	..	..	..	..	..	..	..	..	..	..	..	..
Sedimentation rate, mm./hour	..	..	..	...	..	..	..	..	..	30	22	..	15	..	..
Roentgenograms															
Chest	..	..	—	..	..	—	..	..	..	..	..	—	..	..	..
Skull	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Abdomen	—	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Wrists	..	..	..	..	..	..	..	—	..	..	..	..	..	..	..
Extremities	..	..	..	..	..	..	..	..	—	..	..	..	..	..	..

John [8] and Limper and Miller [5] have collected all cases up to the dates of their reports.

To complete the series, all cases that have been reported, including the present one, are listed in table 4. As in earlier reports, all cases in which the diagnosis of diabetes was questionable have been omitted.

ETIOLOGY

Sex.—Although the present case was that of a female infant, a review of all cases [9] in which the sex was indicated reveals that 27 were boys and 18 girls. This is in agreement with some investigators [2] who found that boys predominate in the early years, so that for the first decade 6.7 per cent were boys and 4.6 per cent girls. However, others [10] have expressed the belief that no significant sex relationship exists in the incidence of juvenile diabetes. Strangely, if the sex incidence is studied from 1922 to the present it will be found that the disease occurred in 16 boys and 14 girls, whereas prior to 1922 it occurred in 11 boys and in only 4 girls (see table 5). It is possible that with the increasing accuracy and improved diagnostic methods of modern medicine the latter figures are the more correct. It may also be that there has been a definite change in the trend of incidence of the disease. Despite two previous studies,[11] in which the incidence in boys predominated, it is felt in view of the foregoing discussion that no sex predilection is shown.

Heredity.—In 12 cases out of 28 (43 per cent) in which information was furnished, a positive familial history of the disease was found. This percentage might well be higher, for it is known that with the increasing duration of the disease the hereditary factor increases; this fact was shown by White,[3] whose figures rose from 20 to 53 per cent as the duration of the condition rose from 2.2 to 10 years.

In comparing the figures of this study with those of previous similar studies,[11] it may be noted that the figure of 43 per cent is definitely higher than those of 35 [7] and 38 per cent [5] which were given in the previous studies. However, other studies [12] in which infants and children were included revealed variations from 17 to 50 per cent.

---

8. John, H. J.: J. Pediat. **6**:211, 1935.

9. Nyström, G.: Svenska läk.-tidning. **29**:1265, 1932.

10. Holt, L. E., Jr., and McIntosh, R.: Holt's Diseases of Infancy and Childhood, ed. 10, New York, D. Appleton-Century Company, Inc., 1933, p. 599. Boyd.[1]

11. Limper and Miller.[5] Lawrence and McCance.[7]

12. (*a*) Toverud, K. U.: Brit. J. Child. Dis. **24**:185, 1927. (*b*) Lion, G., and Moreau, C. P.: Arch. de méd. d. enf. **12**:21, 1909. (*c*) John, H. J.: Ann. Int. Med. **8**:198, 1934. (*d*) Priesel, R., and Wagner, R.: Die Zuckerkrankheit und ihre Behandlung im Kindesalter, Leipzig, Georg Thieme, 1931, p. 12. (*e*) Ladd, W. S.: Growth in Children with Diabetes Mellitus, Am. J. Dis. Child. **32**:812 (Dec.) 1936. (*f*) Collens, W. S., and Grayzel, H. G.: The Management of the Ambulatory Diabetic Child, ibid. **38**:275 (Aug.) 1929. Holt and McIntosh.[10]

TABLE 4.—*Review of Cases of Diabetes Mellitus in Infants Under 1 Year of Age*

Case No.	Author	Age at Onset	Sex	Family History of Diabetes	Symptoms	Laboratory Findings: Glycosuria	Laboratory Findings: Blood Sugar, Mg./100 Cc.	Outcome	Autopsy Observations
1	Hauner: Wchnschr. f. d. ges. Heilk. **21**: 321, 1850	11 mo.	..	..	Loss of weight; polydipsia; polyuria	..	..	Died in 1 mo. in coma	.....
2	Kitselle,[35b] 1852	Few days	M	Negative	Honeyed napkins; polyuria; restlessness; polydipsia; polyphagia; dry skin; extreme emaciation	+	..	Died after 6 mo.	.....
3	Griesinger,[34a] 1850	1 yr.	F	..	.....	+	..	Died	Kidneys enlarged, filled with small abscesses
4	Rosbach,[30a] 1874	8 mo.	F	..	Fall on head, with convulsions and unconsciousness; polydipsia; polyuria; furunculosis; wasting	+	..	Died after 3 mo.	Pancreas not examined
5	Busch: Jahresb. ü. d. Leistung. u. Fortschr. d. ges. Med. **2**: 271, 1876	Under 1 yr.	..	..	Restlessness; wasting; polydipsia	+	..	Died after 23 days	.....
6	Hagenbach,[21a] 1879	8 mo.	M	..	Polydipsia; polyuria; hydrocephalus	+	..	Died after 11 mo.	Tuberculous right pleura; gangrene of lung; chronic internal hydrocephalus
7	Garnerus, H.: Deutsche med. Wchnschr. **10**: 697, 1884	2 mo.	M	..	Polyuria; thirst; failure to gain weight	+	..	Recovered after 3 mo.	.....
8	Dreyfuss,[24b] 1886	1 yr.	..	..	.....	..	..	Died 2 days later	.....
9	Tavaria,[30b] 1893	10 mo.	..	..	Fall from cradle; restlessness; polyuria; polydipsia; honeyed napkins; weakness	+	..	Died in 2 wk.	.....
10	Bell,[35a] 1896	3 mo.	M	Father's aunt diabetic	Polydipsia; general irritation	+	..	Died in 4 days, in coma	Nothing abnormal macroscopically
11	Niehues,[24b] 1896	3 mo.	..	Grandfather diabetic	Abscesses; polyuria	+	..	Died soon afterward	.....
12	Baumel,[27a] 1900	6 mo.	M	Negative	Edema; pruritis; hunger; polyphagia; polyuria	+	..	Recovered after 6 wk.	.....
13	Orloff,[31b] 1901	5 mo.	M	..	Restlessness; polydipsia; polyuria; boils; sacral sore	+	..	Died in few days	Distention of lateral ventricle; pneumonia and enteritis
14	Young,[38c] 1901	5 mo.	M	..	Vomiting; dry skin; emaciation; enlarged kidneys and liver	+	..	Died after 2 mo.	Kidneys and liver enlarged; nothing else abnormal
15	Langstein,[21c] 1909	6 mo.	..	..	Hydrocephalus	+	..	Died	Hydrocephalus
16	Langstein,[21c] 1909	7 days	..	..	Anencephalus	+	..	Died after 3 days	.....

TABLE 4.—*Review of Cases of Diabetes Mellitus in Infants Under 1 Year of Age—Continued*

17	Langstein,[21c] 1909	8 mo.	M	Negative	Dry skin; polydipsia; polyphagia; loss of weight	+	..	Questionable	.....
18	Offergeld, H.: Deutsche med. Wchnschr. **35**: 1226, 1909	1 yr.	..	..	.....	..	..	Died after 3 mo.	Pancreas: round cell infiltration of islets and interstitial tissue
19	Lauritzen, M.: Arch. de méd. d. enf. **13**: 561, 1910	8 mo.	M	..	.....	+ and acetone	..	Died after 3 mo. in coma	.....
20	Cuno, F.: Jahrb. f. Kinderh, **71**: 623, 1910	15 days	..	..	.....	+	200	Died after 15 days	Pancreas atrophic and cirrhotic, but islets normal
21	Heiberg, K. A.: Arch. f. Kinderh. **56**: 406, 1911	3 mo.	M	..	.....	+	..	Died after 3 days	Normal pancreas
22	Eaton, P. J., and Woods, E. B.: Tr. Am. Pediat. Soc. **23**: 244, 1911	6 mo.	..	Grandmother diabetic	Gangrene of toes; polydipsia; wasting; sticky diaper	+ and acetone	..	Died after 2 yr.	.....
23	Knox,[6] 1913	8 mo.	F	Negative	Failure to gain weight; dry skin; fruity odor of breath	+ and acetone	..	Died after 3 wk.	Pancreas normal in size; no excess of fibrous tissue; islets diminished in number and size
24	Funaioli, G.: Riv. di clin. pediat. **17**: 83, 1919	2 mo.	M	Negative	Emaciation	..	287	Died after 3 wk.	.....
25	Kochmann,[35b] 1922	4½ mo.	..	Negative	Failure to gain weight; polyphagia; polydipsia; intertrigo; large stools; vomiting; pallor; poor turgor of skin	+	95-444	Died after 2 mo.	Pancreas: islets few, fatty degeneration. Liver: fatty degeneration, interlobular round cell infiltration and hemosiderosis. Hypophysis: cyst of intermediate lobe
26	Ashby,[43a] 1923	5 mo.	F	Negative	Pyelitis; fever; gangrene of 2 toes; loss of weight; irritability; intolerance of food; frequent colds	+	..	Died some weeks later, in coma	.....
27	Major and Curran,[31] 1925	11 mo.	M	Negative	Restlessness; emaciation; fretfulness; change in lens (cataracts)	+	94-222	Living	.....
28	Ambard, L., and others: Bull. et mém. Soc.méd. d. hôp. de Paris **49**: 547, 1925	Birth	..	Mother diabetic	.....	+	440 Amniotic fluid 214 mg./100 cc.	Died	Pancreas: islands normal but fibrous; lymphocytic infiltration in acini
29	Hartmann, A. F.: M. Clin. North America **9**: 69, 1925	1 yr.	M	..	Acidosis; coma	..	..	Recovered with insulin therapy	.....
30	Schippers, J. C.: Am. J. Dis. Child. **30**: 336 (Sept.) 1925	8 mo.	F	..	Wasting; thirst; polyuria; fever	+ and acetone	82-242	Died after 18 mo.	.....
	de Lange, C.: Am. J. Dis. Child. **31**: 840 (June) 1926	Did autopsy on Schippers' case				..	..	.....	Pancreas normal; fatty degeneration of liver, which contained much glycogen
31	Arndt, H., and Welcher, A.: Ztschr. f. Kinderh. **41**: 518, 1926	3 mo.	M	Negative	Edema of feet and eyelids; pallor; lassitude; loose stools; loss of weight	+	257-299	Died	Liver: fatty degeneration and loss of glycogen in liver cells. Pancreas: fat replacement in glandular cells and islands increased in size; round cell infiltration and acinous atrophy. Spleen: hemosiderosis

TABLE 4.—*Review of Cases of Diabetes Mellitus in Infants Under 1 Year of Age—Continued*

Case No.	Author	Age at Onset	Sex	Family History of Diabetes	Symptoms	Laboratory Findings: Glycosuria	Laboratory Findings: Blood Sugar, Mg./100 Cc.	Outcome	Autopsy Observations
32	Ramsey,[43b] 1926	4 wk. premature	M	Positive, with recovery	Loss of weight; infection of upper respiratory tract; polydipsia; polyphagia; profuse perspiration	+	225-263	Child checked 4 yr. later; dextrose tolerance curve was normal	.....
33	Morton,[24c] 1928	12 mo.	M	Paternal grandmother diabetic	Fretfulness; loss of weight; polyphagia; polydipsia; polyuria	+	136-260	Living; at age of 2 yr. required less insulin, aglycosuria noted	.....
34	Feldman, I.: Centralbl. f. allg. Path. u. path. anat. **42**: 435, 1928	At birth	..	Mother diabetic	.....	+	..	Died after 15 mo.	Pancreas: many enlarged islets, edema and swelling of cells; interacinar fibrosis with lymphocytic and plasma cell infiltration
35	Joslin, E. P.: Treatment of Diabetes Mellitus, ed. 4, Philadelphia, Lea & Febiger, 1928, p. 838	8 mo.	M	Maternal grandmother and aunt diabetic	.....	+	..	Child did well on diet and insulin therapy	.....
36	Lenstrup,[45] 1929	11 mo.	F	Negative	Irritability; anorexia; polydipsia; paresis of lower extremities; hematemesis	+	400	Died after 3 days	Few and poorly developed islets; accumulation of fat at periphery of acini of liver
37	Litchfield and Shermer,[35c] 1930	5 mo.	M	..	Diaper rash	+	420	.....	.....
38	Schretter, G., and Nevinny, H.: Arch. f. Gynäk. **140**: 297, 1930; **143**: 465, 1930	Birth	F	Diabetic mother	.....	..	52-172	Died after 29 days	Congenital cardiac disorder. Pancreas: moderate hyperplasia and hypertrophy of the intertubular cellular structures, with progressive degenerative changes; hypertrophy of islets. Other endocrine glands normal except anterior lobe of pituitary, rich in eosinophils
39	Shelley,[37b] 1931	10 mo.	M	..	Polyuria; polydipsia; polyphagia; stiff diaper; pruritus; perspiration about head	+ and acetone	240-327	Died after 4 mo.	.....
40	Lawrence and McCance,[7] 1931	18 days	F	Negative	Gangrene of skin; loss of weight	+	600	Complete cure	.....

TABLE 4.—*Review of Cases of Diabetes Mellitus in Infants Under 1 Year of Age—Continued*

41	Nyström,[9] 1932 ..?.....	11 mo.	F	Negative	Thirst; loss of weight; weakness; pallor; apathy; vomiting; coma	+	175-392	Died after several days	Pancreas: islets few and small; some scattered areas of necrosis of parenchyma. Bilateral basal bronchopneumonia
42	Strandqvist,[32] 1932	6 mo.	M	..	Abscess of right shoulder; gangrene of edges of abscess; temperature raised; thirst	+	..	Recovered and then dextrose tolerance curve normal	.....
43	Newcomb,[42] 1934	10 mo.	M	Paternal uncle diabetic	Acidosis; diarrhea; bronchitis; otitis; numerous insulin reactions	+	..	Died after 12 days	Gross atrophy of pancreas
44	Lewis and Eisenberg,[36a] 1935 (Negro infant)	Birth	F	..	Failure to gain weight; fever; impetigo contagiosa bullosa (after injection of 5 units of insulin, blood sugar fell to 35 mg. and then rose to 200 mg./100 cc.)	..	280-520	Died after 6 days	Pancreas: increased amount of interacinar fibrous tissue; islets greatly reduced in number. Liver: chronic passive congestion
45	Limper and Miller,[5] 1935.... (Negro infant)	15 days	M	Negative	Constipation; convulsion; loss of weight; gangrene of left foot	+	952	Died	Pancreas: old pancreatitis of head; many islets scarred. Liver: slight fatty infiltration
46	Holland and Holland,[36b] 1936	2 mo.	F	Negative	Failure to gain weight; thrush; loose bowels; impetigo of face and scalp	..	90-360	Living	.....
47	Liège, R.: Progrès méd., 1937, p. 325	10 mo.	M	Negative	Loss of weight	+	..	Living	.....
48	Devine, J.: Arch. Dis. Childhood **13**: 189, 1938	25 days	F	Negative	Failure to thrive	+	542	Died	Hypoplasia of pancreas with great diminution in number of islets
49	White,[3] 1940	.....	M	..	Infections; dwarfism	..	..	.....	.....
50	.....	.....	M	..	Pyelitis	..	..	.....	.....
51	.....	.....	M	..	.....	..	..	.....	.....
52	.....	.....	F	..	Coma; tuberculosis; dwarfism; hepatomegaly	..	..	.....	.....
53	.....	.....	F	..	.....	..	..	.....	.....
54	.....	.....	F	..	.....	..	..	.....	.....
55	.....	.....	F	..	.....	..	..	.....	.....
56	Langlois and Thebandeau,[33] 1941	3 mo.	M	Paternal grandmother diabetic	Ulceration of angioma with infection; anorexia; frequent vomiting; failure to gain weight; poor nutritional state	..	164-174	Recovered	.....
57	Schwartzman, Crusius and Beirne,[40c] 1947	8 mo.	F	Maternal aunt and cousin diabetic	Repeated pulmonary infections; abscess of right buttock; loss of weight	+ and acetone	35-600	Living	.....

Although most reports [3] on persons with diabetes state that paternal heredity played a greater part, in the present series the maternal side predominated, as revealed in table 6.

In most of the cases reported, the racial stock was not emphasized, but the present case occurred in a gentile. Most investigators [13] of this phase have indicated that the incidence in Jews (30 to 44 per cent) is much higher than in gentiles (17.9 to 21 per cent). However, Joslin and associates [2] emphasized that the disease is also common among the Irish, and White [3] stated that 38 per cent of the non-Jewish children in her series had hereditary diabetes.

Other evidence indicating a hereditary factor was reported.[2] Twelve out of 19 pairs (63 per cent) of similar twins had diabetes, whereas only 2 of 25 pairs (7 per cent) of dissimilar twins had the condition.

TABLE 5.—*Distribution of Forty-Five Cases According to Sex*

Date	Male	Female
1850-1922	11	4
1922-1946	16	14
Total	27	18

TABLE 6.—*Distribution of Twenty-Eight Cases*

	Hereditary Factor	
	Positive	Negative
Maternal	5	..
Paternal	4	..
Unspecified	3	..
	12	16

Another study [12c] mentioned 19 pairs of twins, in whom diabetes occurred simultaneously in the members of 3 pairs and within twelve weeks of each other in 4 other pairs.

There seems to be a general agreement [14] that the tendency is transmitted as a recessive factor, and the following possibilities are to be noted:

1. All offspring will have diabetes if diabetic persons intermarry.
2. One-half the offspring will be diabetic if a diabetic person marries a nondiabetic person with a hereditary history.
3. One-fourth the offspring will be diabetic if two nondiabetic persons with the hereditary taint intermarry.
4. None of the offspring will be diabetic if a diabetic person marries a normal person with no hereditary background of the disease.

13. John.[12c] Priesel and Wagner.[12d]
14. Joslin and others.[2] White.[3] John.[12c]

Infections.—Evidence of infection was noted in 18 of 48 cases (37.5 per cent), an observation similar to the findings [5] in a previous study. Although some investigators [15] did not stress infection, John [12c] expressed the belief that it might precipitate diabetes or play havoc in a case in which the disease was already present. He cited Jones, who noted an increase in the incidence of diabetes after an epidemic of influenza.

That infections cause a pronounced increase in blood sugar curves was shown by several investigators,[16] and John [12c] stated the opinion that in a patient with a reduced reserve insulinogenic function infection could initiate diabetes. In 1934 he reported [17] 33 cases of the disease that had occurred within thirty days after an infection, and he based the hyperglycemia during an infection on five possibilities: (1) reduced insulin output; (2) inability of the liver and muscles to store glycogen readily; (3) interference with the action of insulin; (4) nonfunction of the nervous control mechanism; (5) increased epinephrine output. Another report [18] showed that acute infectious diseases had preceded diabetes by ninety days in 23 per cent of the cases.

In view of the fact that infections [19] may precipitate diabetes in predisposed persons within one to three months after onset, it would be advisable to make semimonthly urinalyses during that period after every infection.

Central Nervous System.—In several of the cases reported the diabetes seemed to be associated with cerebral lesions, as illustrated by 2 cases of injury to the head,[20] 3 cases of hydrocephalus [21] and 1 case of anencephalus.[21c] Although the part played by psychogenic factors [22] and by the central nervous system is said to be insignificant, the association of neuropathy with diabetes in 6 out of the 48 cases (12.5 per cent) in this series in which symptoms were listed indicates that it probably plays some part in the derangement of carbohydrate metabolism.

Obesity and Hyperthyroidism.—There were no cases of obesity or hyperthyroidism in this series, a finding in general agreement with

15. Joslin and others.[2] Holt and McIntosh.[10]

16. Goetzky, F.: Ztschr. f. Kinderh. **27**:195, 1920. Lierle, D. M., and Potter, J. J.: Rôle of Chronic and of Subacute Infections in Diabetic Children, Arch. Otolaryng. **14**:432 (Oct.) 1931. Williams, J. L., and Dick, G. F.: Decreased Dextrose Tolerance in Acute Infectious Diseases, Arch. Int. Med. **50**:801 (Dec) 1932.

17. John, H. J.: J. Indiana M. A. **27**:100, 1934.

18. Landabure, P. B., and Magdalena, A.: Día méd. **10**:41, 1938.

19. John.[17] Landabure and Magdalena.[18]

20. (*a*) Rosbach, T.: Berl. klin. Wchnschr. **2**:258, 1874. (*b*) Tavaria, H. K.: Indian M.-Chir. Rev., Bombay **1**:402, 1893.

21. (*a*) Hagenbach: Jahrb. f. Kinderh. **13**:421, 1879. (*b*) Orloff, M. N.: Semaine méd. **21**:192, 1901. (*c*) Langstein, L.: Verhandl. d. Kong. f. inn. Med. **26**:209, 1909.

22. Yendel, B. R., and Benjamin, J. E.: New England J. Med. **234**:556, 1946.

others,[23] who have found such an association unusual in children, although it does occur in adults. However, the curves for chronic infection in children and in adults are identical.

Overnutrition.—Although in several of the cases reported [24] there was a history of the infant's having been on a high carbohydrate diet prior to the detection of the condition, the part this factor plays is doubtful, as some authors [25] have shown that diabetes is independent of food consumption.

SYMPTOMS

From the 48 cases in which symptoms were noted, the following symptoms are listed, in their order of frequency:

Loss of weight		26 (54.2%)
Emaciation, wasting		
Failure to gain weight		
Cutaneous involvement		26 (54.2%)
Dry skin (poor turgor)	5	
Gangrene of skin	5	
Furunculosis	4	
Localized abscess	3	
Intertrigo	3	
Impetigo	2	
Pruritus	2	
Sacral sore	1	
Thrush	1	
Polydipsia		19 (39.6%)
Polyuria		12 (25%)
Gastrointestinal disorders		11 (22.9%)
Loose or large stools	4	
Vomiting	4	
Anorexia	3	
Infections of the respiratory tract		10 (20.8%)
Colds	3	
Pneumonia	3	
Bronchitis	2	
Gangrene of lung	1	
Otitis media	1	
Irritability (restlessness, fretfulness)		8 (16.7%)
Acidosis		8 (16.7%)
Polyphagia		7 (14.6%)
Disorders of the central nervous system		7 (14.6%)
Hydrocephalus	3	
Injury to head	2	
Anencephalus	1	
Convulsion	1	
Coma		6 (12.5%)
Crystalline deposits on diapers (stiff diapers)		4 (8.3%)
Weakness		3 (6.7%)
Pallor		3 (6.7%)
History of diabetes in the mother		3 (6.7%)
Edema		2 (4.2%)
Paresis of lower extremities		1 (2.1%)
Hematemesis		1 (2.1%)
Cataract		1 (2.1%)
Enlarged kidney		1 (2.1%)
Pyelitis		1 (2.1%)
Enlarged liver		1 (2.1%)

23. White.[3] John.[12c]

24. (*a*) Knox.[6] (*b*) Wegeli, E.: Arch. f. Kinderh. **19**:1, 1896. (*c*) Morton, H. B.: Nebraska M. J. **13**:9, 1928. (*d*) Nyström.[9]

25. Joslin and others.[2] White.[3] Mills, C. A.: Diabetes Mellitus: Is Climate Responsible Factor in Etiology? Arch. Int. Med. **46**:569 (Oct.) 1930.

Most authors feel that there is little difference between children and adults in respect to symptoms. However, a review of these cases indicates that there are certain features which, though not diagnostic, should make one suspect diabetes. These are: loss of weight and emaciation, tendency to cutaneous involvement, frequent symptoms of infection of the respiratory tract, irritability and crystalline deposits on, or stiffening of, the diapers. These signs, together with a history of diabetes in the family, should put one on guard against the disease, so that should any of the characteristic signs appear the diagnosis will become self evident.

COMPLICATIONS

Gangrene.—Although White [3] had not reported the occurrence of gangrene in the children and adolescents with diabetes of her series up to 1932, she mentioned it as a complication in her later study,[2] although none of her 7 patients showed it. Surprisingly, in the present series of 57 cases, 6 instances of gangrene were noted (10.5 per cent), making this complication a rather frequent, but undesirable, occurrence.

It must be assumed that in the case of the occurrence of gangrene there was a severe nutritional disturbance in the area involved, based either on the disturbed metabolism or, possibly as in 1 of the cases,[5] on the presence of a thrombus. Although a study [26] of 73 cases of juvenile diabetes over a period of twenty years revealed arteriosclerosis as one of the earliest and most important complications, this change is probably not the basis of gangrene in the present study, for the following reasons: 1. In a series [27] of 98 children with arteriosclerosis, not one was diabetic. 2. Although White [3] mentioned a few children with diabetes in whom atheromatous changes were noted less than one year after the onset of the disease, all but 1 of her 30 patients had had the condition for five years or more. 3. Of 7 patients under 4 years of age on whom autopsy was performed by Warren,[28] none revealed atheroma. 4. In a postmortem study [29] on adults, it was shown that sclerosis increased with age, although it did start ten years earlier in persons with diabetes.

Therefore, because of its relative rarity in children and because of the unlikelihood of its long duration in infants, it would seem that sclerosis cannot explain the gangrenous changes. Probably such changes

26. Eisele, H. E.: The Juvenile Diabetic Patient Surviving Twenty Years, J. A. M. A. **120**:188 (Sept. 19) 1942.

27. Zeek, P.: Juvenile Arteriosclerosis, Arch. Path. **10**:417 (Sept.) 1930.

28. Warren, S.: Pathology of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1930.

29. Lisa, J. R.; Magiday, M.; Galloway, I., and Hart, J. F.: Arteriosclerosis with Diabetes Mellitus: A Study of the Pathologic Findings in 193 Diabetic and 2,250 Nondiabetic Patients, J. A. M. A. **120**:192 (Sept. 19) 1942; correction, ibid. **120**:384 (Oct. 3) 1942.

are due to impaired nutrition on the basis of defective metabolism or to the presence of small thrombi.

Cataracts.—Cataracts are reported by White [3] to have occurred in 15 of her cases of juvenile diabetes. In 9 of these there was associated arteriosclerosis, with its earliest occurrence at the age of 11.9 years. Other authors [30] have reported an incidence of cataract of 14 per cent in 260 diabetic patients under the age of 21 years. In this series, the case [31] reported was detected when the child was 11 months of age, but the condition may have been present earlier. There was no evidence of sclerosis in this case, and a satisfactory response followed surgical and medical care.

Dermatologic Conditions.—In the present case an abscess of the right buttock was noted; in Strandqvist's [32] case, an abscess of the shoulder, and in Langlois and Thebandeau's [33] case, ulceration and infection of a congenital angioma.

Furunculosis [34] was present in 4 cases; intertrigo,[35] in 3 cases; impetigo,[36] in 2 cases; pruritus,[37] in 2 cases; dry skin,[38] in 5 cases; sacral sore,[21b] in 1 case, and thrush,[36b] in 1 case. In addition, one may include in this group 5 of the 6 cases of gangrene described previously.

Thus, there was a total of 26 cases with associated cutaneous disorders. In 5 of these there was dryness of the skin, which may be explained on the basis of dehydration, and in the other 21 cases the lesions occurred as complications. Taking the whole series, these complications occurred in 36.8 per cent. In view of this frequency, might it not seem wise to consider cutaneous disorders as part of the actual picture of diabetes?

Infections.—In many of the cases the diabetes was preceded by or associated with an infection of some kind. In 2 cases it was complicated

30. O'Brien, C. S., and Allen, J. H.: Ocular Changes in Young Diabetic Patients, J. A. M. A. **120**:190 (Sept. 19) 1942.

31. Major, R. H., and Curran, E. J.: Diabetic Cataracts in Infants, J. A. M. A. **84**:674 (Feb. 28) 1925.

32. Strandqvist, B.: Acta pædiat. **13**:421, 1932.

33. Langlois, M., and Thebandeau, R.: Laval méd. **6**:22, 1941.

34. (*a*) Griesinger, W.: Arch. f. physiol. Heilk. **3**:1, 1859. (*b*) Rosbach.[20a] (*c*) Wegeli.[24b] (*d*) Orloff.[21b]

35. (*a*) Bell, W. B.: Edinburgh M. J. **41**:709, 1896. (*b*) Kochmann, R.: Jahrb. f. Kinderh. **99**:20, 1922. (*c*) Litchfield, H. R., and Shermer, B.: Pediatric Bull. **1**:5, 1930.

36. (*a*) Lewis, E., and Eisenberg, H.: Diabetes Mellitus Neonatorum: Report of Probable Case, Am. J. Dis. Child. **49**:408 (Feb.) 1935. (*b*) Holland, C. L., and Holland, E. A.: West Virginia M. J. **32**:407, 1936.

37. (*a*) Baumel, M. L.: Cong. internat. de méd. C.-r. sect. méd. d. enf. **13**:627, 1900. (*b*) Shelley, E. G.: Pennsylvania M. J. **34**:256, 1931.

38. (*a*) Knox.[6] (*b*) Kitselle, J. F.: Kinderheilanstalt **18**:313, 1852. (*c*) Young, W. E.: Arch. Pediat. **18**:198, 1901. (*d*) Langstein.[21c] (*e*) Kochmann.[35b]

with tuberculosis [39]; in 3, with pneumonia [40]; in 2, with bronchitis [41]; in 1, with gangrene of the lung [21a]; in 1, with otitis media,[42] and in 3, with colds.[43] In White's series of cases of diabetes,[3] tuberculin tests revealed a greater than average number of positive reactions.

Acidosis.—Acidosis was noted in at least 6 cases, and coma was the commonest preterminal sign.

Other Complications.—Among the less frequent complications noted were: pyelitis, 2 cases [44]; dwarfism, 2 cases [2]; paresis of the lower extremities, 1 case [45]; hematemesis, 1 case [45]; enlarged liver, 2 cases [46] and enlarged kidney, 2 cases.[47]

MORTALITY

Since White [2] did not mention the outcome in her 7 cases of juvenile diabetes, and in a previous publication [3] noted that 1 of her 4 patients at that time had died, it is felt that, for the sake of exactness, it would be best to leave these cases out of this part of the discussion. Of the remaining 50 cases, there was a fatal outcome in 35 (70 per cent). In

TABLE 7.—*Mortality Rate for Fifty Cases of Diabetes in Infants*

Period		Age, Months				Total
		1 to 3	3 to 6	6 to 9	9 to 12	
1850-1924	No. of cases.....	8	7	5	6	26
	No. of deaths.....	7	6	4	6	23
1925-1946	No. of cases.....	11	2	3	8	24
	No. of deaths.....	7	0	1	4	12

table 7 these fatal cases are broken down into age groups according to two periods—the preinsulin period, extending to 1924, and the insulin period, from 1925 to the present.

From this it can be seen that before insulin was used almost all (88.5 per cent) cases ended fatally, whereas in the more recent period death occurred in only 50 per cent, with the highest mortality occurring in infants under 3 months of age. Yet for the United States as a whole there has been an increase of 27 per cent in the mortality from

39. Joslin and others.[2] Hagenbach.[21a]

40. (*a*) Orloff.[21b] (*b*) Nyström. (*c*) Schwartzman, J.; Crusius, M. E., and Beirne, D.: Present report.

41. Eisele.[26] Schwartzman and others.[40c]

42. Newcomb, A. L.: J. Pediat. **4**:617, 1934.

43. (*a*) Ashby, H.: Lancet **1**:22, 1923. (*b*) Ramsey, W. R.: Tr. Am. Pediat. Soc. **38**:100, 1926. (*c*) Newcomb.[42]

44. Joslin and others.[2] Ashby.[43a]

45. Lenstrup, E.: Klin. Wchnschr. **8**:2244, 1929.

46. Joslin and others.[2] Young.[38c]

47. Griesinger.[34a] Young.[38c]

diabetes [48] for the period of 1930 to 1932, as compared with that of 1940 to 1942. Corresponding figures [48] for New York state revealed an increase of 40 per cent.

However, in general the death rate for the group of infants under 1 year was much higher than that for a series [8] of 214 diabetic patients aged 1 to 20 years, in which 28 (13 per cent) died over a period of fourteen years, and in another series [2] of 1,430 diabetic patients, followed for a longer time, in which 298 (20.8 per cent) died. These facts would lead to the conclusion that diabetes in younger children is more serious, with the highest mortality occurring in infants under 1 year of age.

AUTOPSY REPORTS

A review of the 23 cases in which autopsy reports are given revealed no uniformity; yet the commonest change, occurring in 9 cases (39.1 per cent), was atrophy of the pancreas, with diminution in the size and number of islets. This observation is in conformity with those of Keilty [49] and Conroy.[50] However, in 4 cases (17.4 per cent) no abnormality of the pancreas was noted; in 4 others (17.4 per cent) there was evidence of round cell infiltration, and in 2 (8.7 per cent) hypertrophy of the islets was noted. A similar lack of uniformity in pathologic observations was described in a recent study [51] of 307 diabetic children aged 12 years and older, for whom the autopsy data were inconstant and indefinite.

On the other hand, investigators have noted lesions of the pancreas in anywhere from 88 [52] to 96 [8] to 100 [53] per cent of cases of diabetes and in a report [54] on an older group the author expressed the belief that glomerulosclerosis was the most reliable evidence of diabetes at autopsy. White [3] summarized the pathologic features thus: faulty glycogen distribution in the skin, liver, muscles and heart, and abnormal deposition of fat in the liver, reticuloendothelial system and blood vessels. This description brings to mind the fact that in the present series the only pathologic change of any consistency other than the pancreatic lesions were fatty degeneration, in 4 cases, and glycogen disturbance in the liver, in 2 cases. After giving consideration to all these observations, we feel that, despite the major role that the pancreas plays in diabetes,

48. Sindoni, A., Jr.: Am. J. Digest. Dis. **13**:178, 1946.

49. Keilty, R. A.: Atlantic M. J. **27**:492, 1924.

50. Conroy, M. J.: J. Metabolic Research **2**:367, 1922.

51. Robbins, S. L., and Tucker, A. W., Jr.: New England J. Med. **231**:865, 1944.

52. Opie, E. L.: Diseases of the Pancreas, ed. 2, Philadelphia, J. B. Lippincott Company, 1910.

53. Keilty.[49] Conroy.[50] Allen, F. M.: J. Metabolic Research **1**:4, 1922.

54. Laipply, T. C.; Eitzen, O., and Dutra, F. R.: Intercapillary Glomerulosclerosis, Arch. Int. Med. **74**:354 (Nov.) 1944.

when the entire etiology is revealed, the liver and the endocrine glands will be found to bridge some of the present gaps.

DIAGNOSIS

In the present series, glycosuria was reported in 41 of the 48 cases (85.4 per cent). The blood sugar ranged from 52 to 952 mg. per hundred cubic centimeters. Some dextrose tolerance tests were attempted, as it was noted in some of the earlier reports that blood sugar tests were made one and two hours after meals.

In the present case,[40c] dextrose tolerance tests were the best indicators, because even after the values for the urine and blood approached normal the tolerance curves still revealed a diabetic tendency. Sindoni [48] expressed the opinion that, in general, an interval of two hours after an adequate normal meal is the best for determining a diabetic patient's ability to metabolize food. Some investigators [55] have stated that the routine dextrose tolerance test imposes an artificial strain on the regulating mechanism and that therefore they prefer to use the normal diet.

It is thought that with modern methods every diagnosis should be substantiated by a dextrose or other sugar tolerance curve, after proper preparation of the patient with a normal diet for at least three days.

Some authors [56] have expressed the opinion that the part played by the liver, endocrine glands and nervous system is all-important in this picture. Therefore, in every case a complete work-up of hepatic function should be made to rule out damage to the liver, which may be the main factor.

PROGNOSIS

The younger the child is at onset of diabetes and the longer the condition has persisted prior to detection, the worse the prognosis. However, if the disease in a child is recognized and treated correctly, the prognosis is good, and he should be able to lead a normal life,[57] notwithstanding the possibility [58] of later complications, such as nephropathy, polyneuritis and ocular complications, after the patient has reached 15 to 20 years of age. However, as judged from this series, if the onset occurs when the patient is under 3 months of age, the prognosis is poor.

---

55. Sindoni.[48] Soskin, S.: J. Clin. Endocrinol. **4**:75, 1944.

56. Despich, F.; Hasehohrl, R., and Schonbauer, L.: Wien. klin. Wchnschr. **43**:321, 1930. Houssay, B. A.: Am. J. M. Sc. **193**:581, 1937. Soskin, S.; Essex, H. E.; Herrick, J. F., and Mann, F. C.: Am. J. Physiol. **124**:558, 1938. Soskin, S.: Endocrinology **26**:297, 1940. Cori, C. F.: ibid. **26**:285, 1940. Long, C. N. H.: Proc. Am. Diabetes A. **2**:97, 1942. Sprague, R. G., in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1925, vol. 9, pp. 79-84.

57. Joslin and others.[2] Robbins and Tucker.[51]

58. Rosenbusch, H.: Ann. pædiat. **164**:225 and 281, 1945; **165**:12, 1945.

TREATMENT

The diet to be given the diabetic infant is essentially the same as that of the average infant of the same age. The protective foods,[59] such as proteins, vitamins and minerals, are needed; carbohydrates and fats are variable, and it is recommended that the keto-antiketogenic ratio be kept at 0.5 in early infancy.

For the group [3] under 1 year of age, 50 calories and 1.5 Gm. of protein per pound (456 Gm.) of body weight are recommended. Carbohydrate [5] should be supplied freely, with enough insulin to assure assimilation. Unfavorable reactions to insulin [60] are rather frequent at this age, as was evidenced in the present and in several other cases.[61] In this connection, although White [3] suggested that the relatively small reserve of glycogen in the liver may be the cause, it must be remembered that there are reports [62] of sensitivity to insulin which should also be considered; if sensitivity is present, the use of the antihistamine compounds [63] may find a place in diabetic therapeutics.

Most investigators [64] feel that diabetes in infants is rarely controlled by diet alone, and, therefore, that diabetic infants should receive insulin, with the largest dose [64d] in the evening and the smallest at noon. The average dose [3] at this age is 8 units of insulin injection U. S. P. per day. If protamine zinc–insulin is used, daily examination of the urine is stressed.[58] Although combinations of insulin and protamine zinc–insulin (1:4) have been successfully used,[58] a recent report [65] expressed preference for a combination of insulin and globin zinc–insulin.

Some [66] stated that they favored the "free diet," in which the diabetes is controlled by insulin without dietary restrictions. The diet corresponds to that of a healthy normal child, with enough insulin to assure a generally satisfactory condition, with no evidence of ketosis. Less

---

59. (*a*) Escudero, P.: Día méd. **13**:253, 1941. (*b*) Biskind, M. S., and Schreier, H.: Exper. Med. & Surg. **3**:299, 1945.

60. White.[3] Limper and Miller.[5] Escudero.[59a] Marañón, G.: Med. ibera **22**:498, 1928.

61. Litchfield and Shermer.[35c] Lewis and Eisenberg.[36a]

62. (*a*) Yasuna, E.: J. Allergy **12**:295, 1941. (*b*) McGavack, T. H.; Klotz, S. D.; Vogel, M., and Hart, J. F., read at the twenty-eighth annual meeting of the Association of the Study of Internal Secretions, San Francisco, June 28, 1946.

63. Gastineau, C. F., and Leavitt, M. D.: Proc. Staff Meet., Mayo Clin. **21**:316, 1946.

64. (*a*) White.[3] (*b*) Limper and Miller.[5] (*c*) Escudero.[59a] (*d*) Lichtenstein, A.: Acta pædiat. **24**:171, 1939. (*e*) Blazek, F.: Časop. lék. česk. **70**:1232 and 1255, 1931.

65. Jackson, R. L., and McIntosh, C. B.: Treatment of the Diabetic Child with Particular Reference to the Use of Globin Insulin, Am. J. Dis. Child. **70**:307 (Nov.-Dec.) 1945.

66. (*a*) Sindoni.[48] (*b*) Lichtenstein.[64d] (*c*) Lawrence, R. D.: Acta med. Scandinav. **90**:32, 1938.

emphasis is laid on blood sugar values and on slight or moderate glycosuria, because it [48] is felt that stabilizing the blood sugar level of a diabetic patient does not necessitate its reduction to that of a normal person, and hyperglycemia in these cases is a compensatory phenomenon which facilitates utilization of glucose in the tissues.

In a study [64d] of this dietary method, 50 to 60 patients from 2 to 20 years of age were observed for a period of from two to ten years; their physical and mental development was normal, and it was felt that no harm had come from the blood sugar not being regulated in order to avoid mild glycosuria.

On the other hand, other authors,[67] advocating the complete control method, showed that their advice, when followed, was instrumental in producing maximum growth and development. In evaluating these various therapeutic methods, it would be wise to heed the warning of a recent writer,[68] who cautioned that in any evaluation of diabetic therapy account must be taken of the possibility of unpredictable variations, as evidenced by spontaneous remissions and exacerbations.

SUMMARY AND CONCLUSION

A case of an 8 month old girl with diabetes mellitus is reported.

Fifty-seven cases of diabetes mellitus in infants under 1 year reported in the literature to date are reviewed.

Heredity, infections and disorders of the central nervous system were the main etiologic factors, in the order given.

Early symptoms may be loss of weight, dry or sensitive skin, irritability and/or crystalline deposits on the diapers.

Dermatologic conditions, gangrene, cataract, infections of the respiratory tract, acidosis and coma were the common complications noted.

The commonest observations at autopsy were atrophy of the pancreas, with decrease in size and number of the islands of Langerhans, and fatty degeneration of the liver.

Treatment is based on a diet approaching the normal one, supplemented with insulin and vitamins, as needed.

The earlier the onset of diabetes mellitus, especially if the patient is under 3 months of age, the worse the prognosis; and the longer the disease has persisted unrecognized and without proper treatment, the poorer the outlook.

From the standpoint of the formulation of a prophylactic program, early detection of the disease is most important, so that proper care may be instituted. The following procedures would be advisable: (1) in all cases with a familial history of diabetes: routine dextrose tolerance tests

67. Jackson, R. L., and Kelly, H. G.: J. Pediat. **29**:316, 1946.
68. Glassberg, B. Y.: J. Clin. Endocrinol. **6**:369, 1946.

every two months for the first year and every six months thereafter; (2) during infections: daily urinalyses, with sugar tolerance tests at the onset and the end of the illness; (3) after any infection: routine urinalysis every two weeks for a period of three months, followed by a dextrose tolerance test at the end of that time.

Some may object to these additional precautionary measures on the basis that they require time and cause discomfort and added expense. However, in the profession in which saving of lives is of paramount importance, there can be no acceptance of any measuring rod used to restrain efforts in humanity's cause.

New York Medical College, Flower and Fith Avenue Hospitals.

HISTOPLASMIN SENSITIVITY

Results of Studies of Children in Alabama

STEWART H. WELCH, M.D.†
AND
RUTH BERREY, M.D.
BIRMINGHAM, ALA.

IN A STUDY of children in Tennessee in 1942 Gass and his associates [1] observed that many children exhibiting negative reactions in tuberculin tests had pulmonary calcifications. Later, Christie [2] reported the same observation and began a search for a condition other than tuberculosis as a cause of these lesions. On the basis of reports that in the western states coccidioidomycosis caused pulmonary calcifications, he tested the reactions in his patients to various fungous antigens. Although none of the children gave strongly positive reactions to coccidioidin, many gave positive reactions to histoplasmin, an antigen made from Histoplasma capsulatum.

The purposes of this study were to determine the percentage among the school children in an Alabama city who gave positive reactions to histoplasmin and to tuberculin, and also to study the roentgenograms of those with positive reactions in the tests.

Of 1,200 Negro children in grammar school in a crowded area of the city, 15 per cent had positive reactions in histoplasmin tests and 19 per cent had positive reactions in tuberculin tests. Of 923 white children of families of high income in a suburban area, 4.44 per cent had positive reactions in histoplasmin tests and 8.34 per cent had positive reactions in tuberculin tests. The combined rates for white and Negro children were 10.4 per cent positive reactions to histoplasmin and 14.4 per cent positive reactions to tuberculin.[3]

Of the children admitted to Hillman Hospital for various illnesses 97 were tested with tuberculin and histoplasmin. Of the 77 Negro

† Dr. Welch died Nov. 8, 1946.

1. Gass, R. S., and others: Pulmonary Calcification and Tuberculin Sensitivity Among Children in Williamson County, Tennessee, Am. Rev. Tuberc. **47**:379, 1943.

2. Christie, A., and Peterson, J. C.: Pulmonary Calcification in Negative Reactors to Tuberculin, Am. J. Pub. Health **35**:1131, 1945; Histoplasmin Sensitivity, J. Pediat. **29**:417, 1946.

3. The 1 to 100 histoplasmin was supplied by Dr. Christie. Old tuberculin, in dilution of 1 to 1,000, was used in the tests.

children tested 3 reacted positively to tuberculin and 2 to histoplasmin. Of 20 white children tested, 3 reacted positively to tuberculin and 2 to histoplasmin.

COMMENT

The incidence of sensitivity to histoplasmin was much higher in the Negro children of a crowded area than in the white children of a suburban area. Often 2 or more children of the same family reacted to

Summary of Results

Results of Tests on Nine Hundred and Twenty-Three White Children *

Age (years)	6	7	8	9	10	11	12	13	14	15	16	17
Total number of children	99	124	133	90	143	114	100	98	26	7	6	2
Number positive to tuberculin	2	4	11	7	11	11	11	11	6	2	1	0
Number positive to histoplasmin	1	3	4	7	4	6	8	6	1	1	0	0
Percentage positive to tuberculin	2	3.2	8.3	6.7	7.7	9.6	11	11.3	23.1	28.6	17	0
Percentage positive to histoplasmin	1	2.4	3.0	6.7	2.8	5.6	8	6.1	3.8	14.1	0	0

Results of Roentgenograms of White Children

	Total	With Calcification (No.)	With Calcification (%)
Number positive to tuberculin	60	47	75
Number positive to histoplasmin	41	34	83
Number positive to both	2	2	100

Results of Tests on 1,200 Negro Children †

Age (years)	6	7	8	9	10	11	12	13	14	15	Total	Positive (%)
Number positive to tuberculin	2	12	10	24	30	25	29	28	13	11	229	19
Number positive to histoplasmin	5	4	8	9	30	17	27	19	12	11	180	15

Results of Two Hundred and Twenty-Three Roentgenograms of Negro Children

	Total	With Calcification (No.)	With Calcification (%)
Number positive to tuberculin, negative to histoplasmin	92	46	50
Number negative to tuberculin, positive to histoplasmin	57	29	50.9
Number positive to both	74	41	55.4

* Only 2 white children reacted in both tests.

† Since the ages of the children with negative reactions in th tests are not available, the percentages by age cannot be given.

histoplasmin. While this incidence suggests a contact infection, it may mean only that the children were subjected to the same environment.

No person with clinical histoplasmosis, such as reported by Parsons and Zarafonetis [4] and Davis and Neff,[5] was seen in this area. The only

4. Parsons, R. J., and Zarafonetis, C. J. D.: Histoplasmosis in Man, Arch. Int. Med. **75**:1 (Jan.) 1945.

5. Davis, H. V., and Neff, F. C.: Histoplasmosis in Infancy, Am. J. Dis. Child. **71**:171 (Feb.) 1946.

subject in this series who may have shown clinical signs of histoplasmosis was a 12 year old Negro boy who had a positive reaction in the histoplasmin test and a negative reaction in the tuberculin test. He presented roentgenographic evidence of acute pulmonary infection, pulmonary calcification and bronchiectasis. Examination of the blood, lymph glands and bone marrow did not reveal H. capsulatum.

In tests of 10,580 nurses in eleven cities, Palmer [6] reported that 20.1 per cent were sensitive to histoplasmin. Birmingham has a rather low rate of histoplasmin sensitivity in comparison with other cities in the area between the Mississippi River and the Allegheny Mountains, where the rates varied from 6.3 per cent in St. Paul, Minn., to 65.8 per cent in Kansas City, Mo.

In view of the unreliability of fungous antigens,[7] it has been suggested that sensitivity to histoplasmin may result from other mycotic infections, such as thrush or blastomycosis. Perhaps, since clinicians are becoming more aware of these infections, more cases may be recognized in the acute phase when the causative organisms can be isolated.

SUMMARY

A report is made of the reactions in histoplasmin and tuberculin tests in 1,200 Negro children and 923 white children. Fifteen per cent of the Negro and 4.4 per cent of the white children had positive reactions to histoplasmin; 19 per cent of the Negro and 8.34 per cent of the white children had positive reactions to tuberculin.

Results of roentgenograms of the chest are also given.

NOTE.—Since this paper was submitted there has been a case of histoplasmosis in a 6 month old white child at Children's Hospital, Birmingham, Ala. The organisms were recovered from the bone marrow and peripheral blood. It will be reported in detail at a later date.

2215 Highland Avenue.

6. Palmer, C. E.: Geographic Differences in Sensitivity to Histoplasm Among Student Nurses, Pub. Health Rep. **61**:475, 1946.

7. Emmons, C. W.; Olson, B. J., and Eldridge, W. W.; Studies of the Role of Fungi in Pulmonary Disease, Pub. Health Rep. **60**:1383, 1945.

Case Reports

PSEUDOMONAS AERUGINOSA BACTEREMIA

Summary of Literature, with Report of a Case

G. P. KERBY, M.D.
DURHAM, N. C.

WITHIN recent months a case of Pseudomonas aeruginosa septicemia, with fatal termination, in a 6 month old infant has aroused interest in the subject. Reviews of the literature on this disease have appeared from time to time, but none has been found which assembles all the reported cases of Ps. aeruginosa bacteremia. The present article attempts to bring together all the published reports to date, with a table

Apparent Sources of Infection in Case of Pseudomonas Aeruginosa Bacteremia

Apparent Source of Infection	Adults	Children
Diarrhea *	6 (13.6%)	10 (25.7%)
Cutaneous lesions †	6 (13.6%)	6 (15.4%)
Otitis media ‡	0	5 (12.6%)
Infections of the umbilical cord §	0	4 (10.3%)
Infections of the throat and salivary glands ‖	1 (2.3%)	3 (7.7%)
Postoperative or postinstrumentative infections ¶	14 (31.9%)	1 (2.6%)
Pelvic and urinary infections #	3 (6.8%)	0
Puerperal infections **	3 (6.8%)	0
Unknown source ††	11 (25.0%)	10 (25.7%)
Total classification as to age	44	39

* Ehlers.[1a] Perkins.[1l] Baginski,[1t] Hess.[1u] Dold,[1w] Thayer,[1b'] Ashby,[1c'] Lilley and Bearup.[1d'] Coste and Stefanesco.[1j'] Nieh[1v'] Soeters.[1a''] Present case.

† Barker.[1f] Triboulet and Tolemer.[1h] Perkins.[1l] Eastman and Keene.[1o] Huebener.[1s] Dudden.[1y] Line and Maschke.[1n'] Reichel.[1o'] Epstein and Grossman.[1q'] Bhatnager.[1s'] Kearns.[1u'] Nieh.[1v']

‡ Kossel.[1c] Williams and Cameron.[1d] Baginski.[1t] Dudden.[1y]

§ Wassermann.[1m]

‖ Manicatide.[1g] Dudden.[1y] Coste and Stefanesco.[1j'] Chakravarti and Tyagi.[1y']

¶ Scott.[1g'] Askey.[1h'] Barrington and Wright.[1i'] Mackeen.[1m'] Ewell.[1t'] Nieh.[1v'] Fish and others.[1z'] Brule and others.[1b''] Schutsky and Martin.[1c''] Schein.[1d''] Moragues and Anderson.[1e'']

Barker.[1f] Advier and Alain.[1p'] Bacaloglu and others.[1x']

** Perkins.[1l] Rolly.[1q] Soifer.[1e']

†† Neumann.[1b] Finkelstein.[1e] Manicatide.[1g] Blum.[1j] Brill and Libman.[1k] Benfey.[1r] Clarke.[1v] Dold.[1w] Tsen.[1x] Sonnenschein.[1z] Chiari.[1a'] Lilley and Bearup.[1d'] Gracey.[1k'] Leadingham.[1l'] Alves.[1w']

summarizing the data on the apparent source of infection, i. e., the most likely underlying condition affording a portal of entry to Ps. aeruginosa, with subsequent bacteremia. In some instances the organism was undoubtedly present as a secondary invader in an already damaged site. In other instances it seems probable that Ps. aeruginosa was the initial offending agent. Discussion will be directed principally toward the pediatric aspects of the problem of Ps. aeruginosa bacteremia.

The first 57 reports [1] include only those cases (90 in all) in which Ps. aeruginosa was isolated in pure culture from the blood, either ante

1. (*a*) Ehlers, E.: Hospitalstid. **8**:517, 1890. (*b*) Neumann, H.: Arch. f. Kinderh. **12**:54, 1890. (*c*) Kossel, H.: Ztschr. f. Hyg. u. Infectionskr. **16**:368, 1894. (*d*) Williams, E. P., and Cameron, K.: J. Path. & Bact. **3**:344, 1895. (*e*) Finkelstein, H.: Charité-Ann. **21**:346, 1896. (*f*) Barker, L. F.: Clinical

(Footnote continued on next page)

mortem or post mortem. With 2 exceptions, the postmortem positive cultures were obtained from heart's blood. In 1 instance the positive culture was obtained from the spleen and in another from the liver and kidneys, in the absence of evidence of local lesions in these organs. It is interesting to note as an incidental observation that it was not until

---

Symptoms, Bacteriologic Findings and Postmortem Appearances in Cases of Infection of Human Beings with Bacillus Pyocyaneus, J. A. M. A. **29**:213 (July 31) 1897. (*g*) Manicatide, M.: Jahrb. f. Kinderh. **45**:68, 1897. (*h*) Triboulet, H., and Tolemer: Bull. Soc. anat. de Paris **72**:763, 1897. (*i*) Lartigau, A. J.: Philadelphia M. J. **2**:562, 1898. (*j*) Blum, S.: Centralbl. f. Bakt. **25**:133, 1899. (*k*) Brill, N. E., and Libman, E.: Am. J. M. Sc. **118**:153, 1899. (*l*) Perkins, R. G.: J. M. Research **6**:281, 1901. (*m*) Wassermann, A.: Virchows Arch. f. path. Anat. **165**:342, 1901. (*n*) de la Camp: Charité-Ann. **28**:92, 1904. (*o*) Eastman, J. R., and Keene, T. V.: Ann. Surg. **40**:613, 1904. (*p*) Fraenkel, E.: Virchows Arch. f. Path. Anat. **183**:405, 1905. (*q*) Rolly: München. med. Wchnschr. **53**:1399, 1906. (*r*) Benfey, A.: Med. Klin. **3**:1199, 1907. (*s*) Huebener, S.: Deutsche med. Wchnschr. **33**:803, 1907. (*t*) Baginski, A.: Centralbl. f. Bakt. (Abt. 1) **47**:427, 1908. (*u*) Hess, A. F.: Proc. New York Path. Soc. **60**:158, 1909. (*v*) Clarke, J. M.: Brit. Med.-Chir. J. **21**:4, 1913. (*w*) Dold, H.: Arch. f. Schiffs- u. Tropen-Hyg. **22**:365, 1918. (*x*) Tsen, E. T. H.: China M. J. **34**:389, 1920. (*y*) Dudden, E.: Jahrb. f. Kinderh. **48**:257, 1922. (*z*) Sonnenschein, C.: Klin. Wchnschr. **2**:1758, 1923. (*a'*) Chiari, H.: Zentralbl. f. allg. Path. u. path. Anat. **38**:483, 1926. (*b'*) Thayer, W. S.: Johns Hopkins Hosp. Rep. **22**:1, 1926. (*c'*) Ashby, W. M.; Eldridge, W. W., and Freeman, W.: Chronic Pyocyaneus Infection J. A. M. A. **88**:1307 (April 23) 1927. (*d'*) Lilley, A. B., and Bearup, A. J.: M. J. Australia **1**:362, 1928. (*e'*) Soifer, J. D.: Am. J. Obst. & Gynec. **16**:889, 1928. (*f'*) Pavlica, F., and Grosser, R.: Časop. lék. česk. **68**:1725, 1929. (*g'*) Scott, W. W.: J. Urol. **21**:527, 1929. (*h'*) Askey, J. M.: California & West. Med. **32**:352, 1930. (*i'*) Barrington, F. J. F., and Wright, H. D.: J. Path. & Bact. **33**:871, 1930. (*j'*) Coste, F., and Stefanesco, V.: Bull. et mém. Soc. méd. d. hôp. de Paris **46**:867, 1930. (*k'*) Gracey, D. I.: Brit. M. J. **1**:904, 1930. (*l'*) Leadingham, R. S.: M. J. & Rec. **131**:5, 1930. (*m'*) Mackeen, R. A. H.: Canad. M. A. J. **24**:424, 1931. (*n'*) Line, B. S., and Maschke, A. S.: Three Fatal Cases of Bacillus Pyocyaneus Infection, J. A. M. A. **98**:528 (Feb. 13) 1932. (*o'*) Reichel, H.: Deutsches Arch. f. klin. Med. **28**:299, 1932. (*p'*) Advier, M., and Alain, M.: Bull. Soc. path. exot. **26**:1286, 1933. (*q'*) Epstein, J. W., and Grossman, A. B.: Bacillus Pyocyaneus in Children, Am. J. Dis. Child. **46**:132 (July) 1933. (*r'*) Basnuevo, J. G.: Crón. méd.-quir. de la Habana **60**:15, 1934. (*s'*) Bhatnager, S. S.: J. Roy. Army M. Corps. **63**:331, 1934. (*t'*) Ewell, G. H.: Urol. & Cutan. Rev. **40**:697, 1936. (*u'*) Kearns, J. J.: Malignant Endocarditis Due to Bacillus Pyocyaneus, Arch. Path. **21**:839 (June) 1936. (*v'*) Nieh, C.: Chinese M. J. **50**:1751, 1936. (*w'*) Alves, W.: South African M. J. **11**:230, 1937. (*x'*) Bacaloglu, C.; Cicoulesco, M. A., and Focsa, P.: Bull. Acad. de méd. de Roumanie **2**:481, 1937. (*y'*) Chakravarti, D. N., and Tyagi, N. N.: Indian M. Gaz. **72**:367, 1937. (*z'*) Fish, G. W.; Hand, M. M., and Keim, W. F. Jr.: Am. J. Path. **13**:121, 1937. (*a''*) Soeters, J. M.: Maandschr. v. kindergeneesk. **7**:74, 1937. (*b''*) Brulé, M.; Hillemand, P., and Wolframm, R.: Bull. et mém. Soc. méd. de hôp. de Paris **55**:1163, 1939. (*c''*) Schutsky, M., and Matlin, P.: Pyocyaneus Meningitis, J. A. M. A. **113**:1400 (Oct. 7) 1939. (*d''*) Schein, A. J.: Bacillus Pyocyaneus Osteomyelitis of the Spine, Arch. Surg. **41**:740 (Sept.) 1940. (*e''*) Moragues, V., and Anderson, W. A. D.: Ann. Int. Med. **19**:146, 1943.

about 1928 that antemortem positive blood cultures began to be recorded with considerable regularity in cases of this condition. This does not seem to reflect so much an improvement in the management of these cases as an improvement in bacteriologic study of cases during the life of the patients. It is a relatively infrequent occurrence now for an invasion of the blood stream of a patient to go unsuspected and unstudied from the bacteriologic point of view. As recently as twenty years ago this seems not to have been generally true.

The fifty-eighth through the sixty-third reports [2] deal with a total of 7 cases in which the clinical course and laboratory findings leave little doubt that the patient had Ps. aeruginosa bacteremia. However, in the 2 cases reported by Freeman [2c] and Roberts and Belsey [2e] no positive blood cultures were obtained. In the other cases no mention is made of blood cultures having been made. The table includes only those cases in which the presence of the organism was proved by culture.

REPORT OF CASE

A. C., a white boy aged 6 months, was admitted to the pediatric service with a history of colitis of three and a half weeks' duration. The family history was noncontributory. The child's birth and development had been normal. No immunizations had been made. At 3 weeks of age he had pneumonia and "kept a cold" thereafter. A review of the systems revealed nothing else of significance, except for a history of constipation up to the onset of the present illness. The present illness began three and a half weeks prior to admission, with development of a cold and otitis media (right ear), requiring myringotomy. At that time he also had a "boil" on the side of his abdomen, which was opened by his local physician. Shortly thereafter, there was sudden onset of vomiting, anorexia and diarrhea. The diarrhea continued despite treatment by several local physicians which included change of diet and, perhaps, a course of sulfonamide therapy. There was a 7½ pound (3,402 Gm.) loss of weight in the week prior to his admission. He was referred to the Duke Hospital for treatment.

On his admission the temperature was 37.4 C. (99.3 F.), the pulse rate 144 and the respiratory rate 30. The patient was emaciated and appeared chronically ill. The skin was pale, smooth and moderately dry. The right ear drum was slightly hyperemic, as was the pharynx. The abdomen was rather protuberant. The rest of the the physical examination revealed nothing abnormal. The hemoglobin content on admission was 11 Gm. per hundred cubic centimeters; the red blood count was 4,860,000, and the white blood count, 8,360, with a differential formula of 37 per cent polymorphonuclear leukocytes, 1 per cent stab forms, 59 per cent small lymphocytes and 3 per cent monocytes. Urinalysis showed a trace of acetone and a rare white blood cell per high power field. The stool was clay white, soft and semiformed and showed no mucus, pus, parasites or ova. The benzidine test for blood and tests for fat gave negative results. No pathogens were found in the stool on culture. Serologic tests for syphilis gave negative reactions. The carbon dioxide–combining power of the serum on the sixth hospital day was 49 volumes

2. (*a*) Waite, H. H.: J. Infect. Dis. **5**:542, 1908. (*b*) Groves, E. H.: Brit. M. J. **1**:1169, 1909. (*c*) Freeman, L.: Ann. Surg. **64**:195, 1916. (*d*) Gaucher-and and Pigeaud: Bull. Soc. d'obst. et de gynec. **17**:74, 1928. (*e*) Roberts, J. E. H., and Belsey, R.: Brit. M. J. **2**:1276, 1937. (*f*) Allin, A. E.: Canad. M. A. J. **44**:288, 1941.

per cent. This test repeated the next day showed 38 volumes per cent. Repeated cultures of the stool revealed no pathogens.

On admission the patient was placed on a formula consisting of equal parts of evaporated milk and water with the addition of 0.75 per cent lactic acid and 6 per cent casein, 120 cc. to be given every four hours. "Pablum" was given twice a day, and accessory vitamins, consisting of ascorbic acid, 25 mg.; percomorph liver oil N.N.R., 15 drops, and ½ tablet (each containing 5 mg. thiamine hydrochloride, 5 mg. riboflavin, 25 mg. nicotinamide, 2 mg. calcium pantothenate and 30 mg. ascorbic acid) every day. For two days there was no diarrhea, vomiting or elevation in temperature. He received three transfusions of 75 cc. of whole citrated blood, after which his hemoglobin content was 14.1 Gm. per hundred cubic centimeters. During these first three days he gained 200 Gm. (7 ounces). However, he then began to have an irregular fever, the temperature on the eighth day in the hospital reaching 39.9 C. (103.8 F.), and a watery diarrhea developed, with from two to ten grayish, watery stools each day. Vomiting became severe. At this time his right ear drum was thought to be bulging, and a myringotomy was performed; however, there was no discharge. A blood culture made on the eighth day in the hospital yielded no growth. Treatment with penicillin was started, 2,000 units being given every two hours but he was not given any sulfonamide drug because his white blood cell count had dropped to 6,420. The differential count was essentially as it was on his admission. Administration of penicillin was continued throughout his stay in the hospital. No streptomycin was available for use during his illness. His temperature curve was septic in type thereafter, with maximum daily elevations ranging from 38.7 to 39.8 C. (101.7 to 103.6 F.) after the thirteenth day in the hospital. He was taking little of his formula and vomited most of that taken. A change in formula did not result in improvement. On several occasions he was given fluids subcutaneously and intravenously, with sixth-molar lactate solution when indicated by the low carbon dioxide-combining power. He was also given three transfusions of plasma. On the twelfth day in the hospital he received a single dose of 0.5 Gm. of sulfadiazine by mouth. This medication was not repeated. During his short stay there developed oral lesions typical of thrush which were painted twice daily, first with methylrosaniline chloride U.S.P. and later with dilute solution of formaldehyde U.S.P. (1:200). On the fourteenth and eighteenth days in the hospital, blood cultures showed innumerable colonies of Ps. aeruginosa. Several days before death pyogenic lesions appeared over the skin of the abdomen and on the third finger of his right hand. On the day of his death his white blood cell count had dropped to 1,800, and the differential formula showed no mature polymorphonuclear leukocytes, 16 per cent stab forms, 22 per cent juvenile forms, 1 per cent blast cells and 61 per cent small lymphocytes. His carbon dioxide–combining power was 25 volumes per cent, although he was given 100 cc. of sixth-molar lactate solution intravenously and 140 cc., subcutaneously. About one hour after the fluid was given the patient died, apparently of respiratory failure, on the eighteenth day in the hospital.

On postmortem examination the right middle ear appeared injected. No exudate was present. The lower lobes of both lungs showed focal pneumonia, gray consolidation and focal necrotizing pneumonia (agranulocytic). There was moderate hyperplasia of the reticuloendothelial elements and absence of granulocytes and blast cells. The ileum showed lymphoid hyperplasia but no ulcerative lesions. In the colon microscopic areas of ulceration were observed, associated with regional thromboarteritis and thrombophlebitis. In these regional areas masses of gram-

negative rods were seen within the reactive sites. Bacteriologic study of the spleen and both lungs revealed in each a heavy growth of Ps. aeruginosa and a moderate growth of Escherichia coli.

COMMENT

The table attempts to classify broadly the 91 cases of proved Ps. aeruginosa bacteremia according to apparent source of infection and to compare cases of the disease in adults with those in children in this respect. Use of percentages in so small a series of cases is admittedly open to criticism. However, even though the percentages given have to be accepted with reservation, they do serve the purpose of giving, within rough limits, a basis for a comparison of incidence in these two age groups. De la Camp's case [1n] cannot be classified either as to source or as to age group. Seven additional cases [3] cannot be classified as to age group and so also are omitted.

Bacteremia following operative or instrumentative procedures in fields infected with Ps. aeruginosa predominates in the adult group and is infrequent in the pediatric group. In 10 of the 15 such cases reported, bacteremia followed urologic procedures. In the single case in the pediatric group, the bacteremia developed after mastoidectomy subsequent to an otitis media [1v'] caused by Ps. aeruginosa. Unlike the other cases classified under otitis media, there is no way of judging what the course of events would have been in this instance without surgical intervention.

Two cases of otitis [1p] could not be classified as to age group. Despite this omission, infections of the middle ear were significant as a source of Ps. aeruginosa bacteremia in the pediatric group. The same was true of the cases in which diarrhea was the presenting symptom of illness and in which the only apparent entry to the blood stream was from the gastrointestinal tract. In the pediatric group, evaluation of all these cases as to the source of bacteremia was made difficult by the fact that diarrhea is frequently associated with an acute febrile illness in early childhood. The case of the child with an unexplained diarrhea who is found subsequently to have otitis media or other focus of acute infection is a familiar one. Rather commonly, no focus of infection can be demonstrated, and the diarrhea remains unexplained. If Ps. aeruginosa bacteremia develops in such a child, it is difficult to say whether a discovered or an undiscovered focus of infection served the organism as a portal of entry into the blood stream or whether the organism entered through lesions in the gastrointestinal tract, with Ps. aeruginosa acting either as the initial agent causing the diarrhea or as a secondary agent which became active after the onset of diarrhea caused by an infection elsewhere. Careful bacteriologic and histologic studies frequently give the answer to this question, as is illustrated in the case reported here: The infant had a history of acute otitis media, necessitating myringotomy. There was no report of a bacterial culture having been made at this time. The following week saw the onset of an acute gastrointestinal disorder. Postmortem studies seemed to demonstrate that the portal of entry of Ps. aeruginosa into the blood stream was through a lesion in the colon. The studies suggested that the gastrointestinal disorder

3. Lartigau.[1l] Fraenkel.[1p] Pavlica and Grosser.[1f'] Basnuevo.[1r'] Bhatnager.[1s']

was secondary to the acute otitis media and that Ps. aeruginosa was a secondary invader in the gastrointestinal tract.

Obviously, Ps. aeruginosa bacteremia cannot be considered a condition commonly encountered in pediatric practice. However, when it does occur, the child is very ill indeed, and frequently dies. The organism appears to be unaffected by penicillin. Results with the sulfonamide drugs are variable. However, streptomycin now gives promise of being an effective agent in combating infections of this type. Therefore, when a case is encountered in which unexplained diarrhea, or diarrhea associated with an acute focal infection, fails to respond to the usual therapeutic measures, so that, instead, the illness begins to run a septic course, it would seem worth while to consider in the differential diagnosis the possibility of Ps. aeruginosa septicemia.

In 5 of the 90 reported cases agranulocytosis [4] or granulocytopenia [5] developed during the course of the infection. Although not all the case reports include hematologic studies, it is possible, nevertheless, to comment that a change in the granulocyte series was not the usual complication. Granulocytopenia apparently cannot be considered as a characteristic development in cases of Ps. aeruginosa septicemia.

SUMMARY

Ninety reported cases of Ps. aeruginosa bacteremia verified by antemortem or postmortem blood cultures are reviewed as to the apparent source of infection. An additional case in an infant is reported.

Of 39 cases of Ps. aeruginosa bacteremia in children, the apparent source of infection was the gastrointestinal tract, in 25.7 per cent; cutaneous lesions, in 15.4 per cent, and otitis media, in 12.6 per cent.

Of 44 cases of the infection in adults, Ps. aeruginosa bacteremia occurred after operative or instrumentative procedures in 31.9 per cent of the cases, being commonest after urologic procedures.

While not all the case reports include hematologic studies, granulocytopenia was not observed to be a characteristic development in Ps. aeruginosa bacteremia. Of the 90 cases reviewed, agranulocytosis was reported in only 2 cases and granulocytopenia in 3 cases.

Duke University.

4. Mackeen.[1m] Nieh.[1v]

5. Pavlica and Grosser.[1f] Askey,[1h] Epstein and Grossman.[1q]

News and Comment

PERSONAL NEWS

Appointment of Dr. Tyree C. Wyatt as Chairman of Department of Pediatrics, Syracuse University College of Medicine.—Announcement has been made that on July 1, 1947, Dr. Tyree C. Wyatt was appointed professor of pediatrics and chairman of the department of pediatrics of Syracuse University College of Medicine. Dr. Wyatt was graduated from Wake Forest College, Wake Forest, N. C., and received his M.D. degree from Syracuse University College of Medicine in 1922. From 1922 to 1927 he was affiliated with the department of pathology of Syracuse. This association was followed by appointments at Peter Bent Brigham Hospital, Boston, and at New York Nursery and Childs Hospital and Cornell University Department of Pediatrics, New York. In addition to his new duties, he will continue to direct the work in pediatric pathology at Syracuse Memorial Hospital.

Rocky Mountain Pediatric Society Honors Dr. Gengenbach at Dinner.—On Oct. 18, 1947, at the University of Colorado Medical Center, a dinner was given for Dr. Franklin P. Gengenbach, the first professor of pediatrics at the university and one of the founders of the Rocky Mountain Pediatric Society, which sponsored the dinner. At the dinner a library, to be named the Gengenbach Pediatric Library, was presented to the medical school by Dr. William Wiley Jones, of Denver.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

THE RELATIVE EFFICIENCY OF DIFFERENT FORMS OF INTRAVENOUSLY ADMINISTERED NITROGEN ON NITROGEN BALANCE AND AMINO ACID EXCRETION. WARREN M. COX JR. and ARTHUR J. MUELLER, J. Nutrition **31**:581 (May) 1946.

The authors conducted a comparative study of nitrogen retention when an enzymic hydrolysate and mixtures of amino acids were given intravenously to protein-depleted dogs. It was noted that the essential amino acid composition of a substance will not necessarily determine its value. In the dogs, 7.65 Gm. of essential amino acids administered as the hydrolysate was almost as effective as 16.23 Gm. of the crystalline essential acids. At higher levels, but at the same ratio of intake, the smaller quantity from the hydrolysate was much more effective in accomplishing nitrogen retention. This difference was partially explained by the presence of unnatural isomers in the synthetic amino acids, partially by rapid excretion and also by the requirement of the animal body for certain amino acids which are not classified as essential. The formation of new protein requires the presence of a number of unessential amino acids, and if they are not specifically supplied in the diet the essential acids will be utilized to form them. Nausea and vomiting accompanied the rapid administration of protein hydrolysates and amino acids.

FREDEEN, Kansas City, Mo.

SOME INTERRELATIONSHIPS OF DIETARY IRON, COPPER AND COBALT IN METABOLISM. A. E. H. HOUK, A. W. THOMAS and H. C. SHERMAN, J. Nutrition **31**:609 (May) 1946.

The authors studied the results of five diets with varying ratios of iron, copper and cobalt fed to young healthy albino rats, and report the effect of the three metals on food intake, growth, hemoglobin level and metal storage and retention.

FREDEEN, Kansas City, Mo.

PHOSPHORUS METABOLISM OF PRESCHOOL CHILDREN. BEULA V. MCKEY, MARIE FOLSOM CLARK, FRIEDA L. MEYER and MILICENT L. HATHAWAY, J. Nutrition **31**:657 (June) 1946.

The authors studied phosphorus metabolism in 8 preschool children on phosphorus intakes of 896 to 1,374 mg. per day, or 55 to 76 mg. per kilogram per day. The values for retentions per kilogram of body weight varied from 3.5 to 10.8 mg. per kilogram. None of the supplements, ascorbic acid, potassium citrate or orange juice, caused significant alterations in phosphorus retentions.

FREDEEN, Kansas City, Mo.

NITROGEN METABOLISM OF PRESCHOOL CHILDREN. MARION S. LEW, DOROTHY D. CLAGETT, FRIEDA L. MEYER and MILICENT L. HATHAWAY, J. Nutrition **31**:665 (June) 1946.

Nitrogen metabolism was studied by the authors in 8 preschool children on protein intakes of between 45 and 58 Gm. per day. The basal diet was supplemented with ascorbic acid, potassium citrate and orange juice as indicated.

The percentage retention of nitrogen was highest when a supplement of orange juice was added to the diet.

FREDEEN, Kansas City, Mo.

THE COMPARATIVE GROWTH-PROMOTING VALUE OF THE PROTEINS OF WHEAT GERM, CORN GERM AND OF SOME OTHER PROTEIN FOODS OF PLANT AND ANIMAL ORIGIN. D. BREESE JONES and KATHERINE D. WIDNESS, J. Nutrition **31**:675 (June) 1946.

Growth-promoting values of the proteins of wheat germ and corn germ were determined by the authors from feeding experiments with young albino rats. In general, the protein values of the following materials, determined by both the *ad libitum* and the paired feeding methods, were observed to rank in descending order: egg powder, wheat germ, corn germ and soybean flour.

FREDEEN, Kansas City, Mo.

STUDIES ON THE COMPARATIVE NUTRITIVE VALUE OF FATS: VII. GROWTH RATE WITH RESTRICTED CALORIES AND ON INJECTION OF THE GROWTH HORMONE. HARRY J. DEUEL JR., CORNELIA HENDRICK and MARY E. CROCKETT, J. Nutrition **31**:737 (June) 1946.

The authors observed that when a preparation of the growth hormone was injected the augmented growth of the rats receiving the vegetable fat diets was as great as, or greater than, that of the rats receiving the butter diet. Increased growth does not occur when growth hormone is injected in rats receiving deficient (i. e., vitamin A–N free) diets; the period of survival is also decreased. Various vegetable fats and margarine have an ability equal to that of butter in supporting added requirements of growth. When the growth hormone was injected, a greater efficiency in the utilization of the foodstuffs needed for growth was observed.

FREDEEN, Kansas City, Mo.

BIOLOGICAL VALUE OF PROTEINS IN RELATION TO THE ESSENTIAL AMINO ACIDS WHICH THEY CONTAIN: IV. ANALYSIS OF FIFTEEN PROTEIN FOODS FOR THE TEN ESSENTIALS. LESLIE E. EDWARDS, ROBERT R. SEALOCK, WILLIAM W. O'DONNELL, GRANT R. BARTLETT, MARION B. BARSLAY, ROBERT TULLY, RITA H. TYBOUT, JEAN BOX and JOHN R. MURLIN, J. Nutrition **32**:597 (Dec. 10) 1947.

The authors describe the methods used, and the controls employed for their verification, in the analysis of fifteen high protein foods for the ten essential amino acids.

FREDEEN, Kansas City, Mo.

MASTITIS DURING THE NURSING PERIOD AND ITS EFFECT ON THE INFANT. L. CUSMANO, Riv. di clin. pediat. **40**:193 (April) 1942.

The problem of mastitis, including the prophylaxis and treatment, is discussed. Sulfanilamide and estrogenic substances are recommended to relieve the infection and to lessen the secretion of milk.

HIGGINS, Boston.

Vitamins; Avitaminoses

METABOLISM OF WOMEN DURING THE REPRODUCTIVE CYCLE: VIII. THE UTILIZATION OF THIAMINE DURING LACTATION. CHARLOTTE RODERUCK, HAROLD H. WILLIAMS and ICIE G. MACY, J. Nutrition **32**:249 (Sept. 10) 1946.

The authors studied the thiamine intake for five day periods, its secretion in twenty-four hour collections of milk and its daily excretion in the urine of normal multiparas during the first ten days post partum and at various intervals during the period of mature milk production. Qualitatively, the food intakes of the mothers were comparable, but appetite determined the quantity. With an average intake of 1.1 mg. of thiamine hydrochloride per day, the average daily secretion of thiamine in milk increased from 1 microgram, on the first day, to 95 micrograms on the tenth day. The urinary excretion ranged from 200 micrograms, on the first day, to 145 micrograms, on the ninth day. During the period of highest excretion of thiamine in milk, two to three months post partum, the amount of thiamine in the milk averaged only 8 per cent of the intake.

FREDEEN, Kansas City, Mo.

METABOLISM OF WOMEN DURING THE REPRODUCTIVE CYCLE: IX. THE UTILIZATION OF RIBOFLAVIN DURING LACTATION. CHARLOTTE RODERUCK, MARGARET N. CORYELL, HAROLD H. WILLIAMS and ICIE G. MACY, J. Nutrition **32**:267 (Sept. 10) 1946.

Riboflavin was determined in composites exactly representing the food intakes of healthy nursing mothers during five day periods and in twenty-four hour collections of their milk and urine during the same intervals post partum. The authors studied the utilization of riboflavin by these multiparous subjects, who received diets of comparable quality in amounts which satisfied their appetites. The average daily intake of riboflavin was 3.1 mg. per day. Secretion of riboflavin in milk increased with milk production from an average of 0.01 to 0.49 mg. per day during the first ten days post partum. The average daily secretion of riboflavin in mature milk was 0.29 mg. While secretion of riboflavin paralleled the volume of milk, the inclusion of liver in the diet of the fifth day of each five day period provided an intake of riboflavin 50 per cent greater than the mean intakes for the other four days. This produced only slight increases in secretion and excretion on the fifth day post partum but augmented the amounts of riboflavin in milk and urine collected on the fifth day of all other five day periods.

FREDEEN, Kansas City, Mo.

THE NUTRITIVE VALUE OF CANNED FOODS: CHANGES IN THE VITAMIN CONTENT OF FOODS DURING CANNING. N. B. GUERRANT, M. G. VAVICH, O. B. FARDIG, R. A. DUTCHER and R. M. STERN, J. Nutrition **32**:435 (Oct. 10) 1946.

The authors made studies of the vitamin retention of canned foods as produced under commercial canning practices.

FREDEEN, Kansas City, Mo.

URINARY CALCIUM IN SICK AND WELL CHILDREN AFTER ADMINISTRATION OF IRRADIATED ERGOSTEROL AND AFTER EXPOSURE TO ULTRAVIOLET RAYS. B. EDILIO, Riv. di clin. pediat. **39**:599 (Nov.) 1941.

The excretion of calcium in the urine of normal and rachitic children was invariably lessened both by feeding therapeutic doses of irradiated ergosterol and by exposure to ultraviolet rays.

HIGGINS, Boston.

ASCORBIC ACID METABOLISM IN PREMATURE INFANTS. FERNANDA CHEMI, Riv. di clin. pediat. **40**:239, 1942.

The metabolism of ascorbic acid was studied in 11 premature infants during the first weeks of life. The mothers of the premature infants had a lower percentage of ascorbic acid in their milk than had the mothers with full term infants. About one-half the ascorbic acid ingested by these premature nurslings was excreted in the urine. When they were given supplementary ascorbic acid, there was a pronounced increase in its retention.

HIGGINS, Boston.

Hygiene; Growth and Nutrition; Public Health

NATIONAL SURVEY OF STATE LEGISLATIVE PROVISIONS FOR THE SPEECH DEFECTIVE CHILD IN THE PUBLIC SCHOOL. FRANCES WELBORN FESLER, Quart. J. Speech **32**:349, 1946.

A letter was sent to the director of each state department of education and to the supervisor of schools in Washington, D. C., asking for information concerning legislation enacted by the state for the education of its speech-defective children. Only 6.1 per cent of the states and the District of Columbia have specific legislative provisions for speech rehabilitation in public schools. But 16.3 per cent of the states, representing 22 per cent of the total school population, have included those with speech defects in the handicapped children to receive special education in the public schools. In another 16.3 per cent of the states, comprising 17.3 of the total school population, speech-defective children are not mentioned in legislative provisions, but are included in the programs for handicapped children. In 10.2 per cent, representing 9.2 per cent of the total school population, programs have been proposed or considered. In about 50 per cent of the states, or 46 per cent of the total school population, there is no mention of programs, provisions or proposed legislation. In 61 per cent of the states there are no programs or formal provisions for programs at present. Thirty-nine per cent of the states were taking care of their speech-defective children by specific inclusion of such children in the laws regarding handicapped children or by liberal interpretation of these laws.

PALMER, Wichita, Kan.

Prematurity and Congenital Deformities

DIET OF MOTHER AND HYDROCEPHALUS IN INFANT RATS. L. R. RICHARDSON and A. G. HOGAN, J. Nutrition **32**:459 (Oct. 10) 1947.

Female rats were fed a synthetic diet to which thirteen vitamins had been added. The vitamin mixture did not contain ascorbic acid or pyridoxine. and the diet contained no unrecognized vitamins unless they were present as contaminants. Hydrocephalus developed in nearly 2 per cent of the offspring. Presumably, this abnormality was the result of a nutritional deficiency.

FREDEEN, Kansas City, Mo.

FAT METABOLISM OF PREMATURE INFANTS. A. GALLEOTTI-FLORI, Riv. di clin. pediat. **39**:617 (Dec.) 1941.

Eleven twenty-four-hour experiments on the fat and nitrogen balance of 8 premature infants, weighing 1,460 to 2,800 Gm. and receiving mother's milk, are reported. Values for fat retention were between 88 and 99.5 per cent, the mean being 96.3 per cent. From 51 to 84 per cent—a mean of 74 per cent—of the nitrogen

absorbed was retained by the body. Although the absorption and retention of fat were good, they were not necessarily accompanied with a gain in the body weight.

HIGGINS, Boston.

Newborn

SO-CALLED ERYTHROBLASTOSIS OF FETUS AND NEW-BORN: REPORT OF CASE OF ICTERUS GRAVIS. R. GIUNTINI, Riv. di clin. pediat. **39**:539 (Oct.) 1941.

A case is presented of a newborn baby with icterus gravis who recovered. In the author's opinion, the congenital edema, icterus gravis and severe anemia of the newborn have a single and common cause, which involves the whole body but may be especially manifest in one particular organ; these conditions are not necessarily fatal.

HIGGINS, Boston.

Acute Contagious Diseases

THE HEART IN ACUTE ANTERIOR POLIOMYELITIS. W. I. GEFTER, W. G. LEAMAN JR., P. F. LUCCHESI, I. E. MAHER and M. DIVORIN, Am. Heart J. **33**:228 (Feb.) 1947.

The authors investigated the cardiac status of 467 patients with acute anterior poliomyelitis.

Of 226 patients who were studied electrocardiographically, 32 (14.2 per cent) showed abnormalities in the electrocardiogram. These changes were noted more frequently in patients with a severe form of the disease. Necropsy was performed in 6 of 11 fatal cases, and pathologic changes in the myocardium were observed in 5.

GIBSON, Chicago.

AN EFFECTIVE CONTROL PROGRAM FOR RABIES. ROBERT H. BROAD and ALEXANDER ZEISSIG, New York State J. Med. **46**:167 (Jan. 15) 1946.

There was an unusual number of cases of rabies in New York state in 1945. Tompkins county was in the path of the spreading wave of the disease. A group from the faculty of the New York State Veterinary College at Cornell University initiated a program to inform veterinarians, physicians and the lay public of the known facts regarding the disease. This committee worked in close cooperation with the health officers of Ithaca and the other officers of the county.

The following recommendations were put into force:

1. The night quarantine on dogs was strictly enforced. In order to accomplish this, extra dog wardens were appointed. 2. Wardens were instructed to pick up and dispose of unwanted stray dogs, this class of dogs being the principal disseminators of rabies. 3. The public was instructed regarding rabies. 4. Persons were requested to report all dog bites and to have them properly treated. 5. Procedures to be employed should rabies appear in the area were discussed.

The public was instructed by means of radio talks, addresses before service clubs and other groups. Excellent cooperation was obtained, and many unwanted dogs were eliminated. Finally, large numbers of dogs were vaccinated privately against rabies. It was necessary to avoid any criticism for cruelty or overzealousness on the part of officers. The disease developed in 2 dogs and a fox a few months later. The previous preparation was of great value, and excellent cooperation was secured from the public.

To aid in securing public cooperation a "rabies council," composed of the district state health officer, chairman; one of the town health officers, the city health officer, the county dog warden, and two dog owners, was selected.

Other methods used in the control of the infection are discussed, especially the appropriation of money by the county for the establishment of free vaccination clinics. The disease quickly disappeared from the county, and no cases had been present for six months prior to this report.

AIKMAN, Rochester, N. Y.

ACID-BASE EQUILIBRIUM IN CASES OF PERTUSSIS. E. COMOLLI and C. TRAVAGLIO, Riv. di clin. pediat. **44**:257 (May) 1946.

Determinations of the alkali reserve and of the chlorides of the blood of 25 children with pertussis revealed that the ratio of chlorides of the cells to chlorides of the plasma was above the normal value of 0.6 for 14 children and under the normal value for 6 children. These data are regarded as indicating "compensated acidosis."

HIGGINS, Boston.

PROPHYLAXIS OF PERTUSSIS. F. FURBETTA, Riv. di clin. pediat. **44**:294 (May) 1946.

Statistics cited from the literature are used to indicate the desirability of vaccine prophylaxis against pertussis.

HIGGINS, Boston.

VARIATIONS IN REDUCING SUBSTANCES AND ASCORBIC ACID IN URINE OF PATIENTS WITH SCARLET FEVER. L. NASSI, Riv. di clin. pediat. **39**:548 (Oct.) 1941.

In the first few days of scarlet fever, the patient excretes a larger amount of ascorbic acid in the urine than normally; the excretion of ascorbic acid soon falls to normal, to increase again during the third to fifth week of the disease. The greater excretion occurs irrespective of whether or not the patient has nephritis and is thought to be due to the increased permeability of the renal capillaries. Therefore, patients with scarlet fever should receive an abundant supply of ascorbic acid and vitamin P (a mixture of flavones, eriodictyol and hesperidin) during their illness.

HIGGINS, Boston.

INFLUENZA VIRUS AND PROTECTIVE IMMUNITY. P. LUCIANI, Riv. di clin. pediat. **41**:280 (May) 1943.

Clinical observations were made at an orphanage in Perugia. Each child had an influenzal infection an average of three to four times a year. Children with the exudative diathesis had the infection oftener, four to five times a year. Tests on mice revealed that 41 per cent of the children had immune antibodies in their blood three months after the infection. The older the children, the higher the percentage showing immune antibodies at this period. Breast-fed infants maintained immunity longer than the bottle-fed infants.

HIGGINS, Boston.

DISTRIBUTION OF THE PARALYSES IN ACUTE ANTERIOR POLIOMYELITIS. LÉON LEVIT, Rev. Soc. pediat. d. litoral **10**:260 (Sept.-Dec.) 1945.

The author discusses the localization of the pareses and paralyses in a series of 41 cases. In 27 of these cases the patients were observed in the acute and subacute stages, whereas in 14 cases the disease was in the chronic stage and the typical deformities were present. In the first group, 10 cases were characterized by paraplegia of both legs; 1 case, by hemiplegia and paralysis of the opposite

leg, and 5 cases, by quadriplegia (both arms and both legs); 2 cases were of the ascending form, involving the limbs and neck, and in 1 case the disease began with paralysis of the soft palate and the facial muscles, gradually extending to the neck, trunk and limbs. In 3 cases the muscles of the hip were involved. In the group of chronic cases occurred such deformities as talipes equinovarus, talipes equinovalgus and talipes equinocavus; muscular atrophies, and subluxations and luxations due to deformities of the joints; in 3 cases deformities of the vertebral column were observed.

SOLMITZ, CHICAGO.

VELOCITY OF DIFFUSION OF AN ELECTROLYTE (HYDROGEN CHLORIDE) IN SERUM GEL IN INTERNAL LEISHMANIASIS. ARMANDO CARNEVALE, Pediatria **55**:81 (Jan.-March) 1947.

The author estimated the rapidity of diffusion of an electrolyte (hydrogen chloride) in frozen serum of 15 children with visceral leishmaniasis. In all but 1 of the patients he observed a remarkable increase in the rate of diffusion (from 48 to 54 mm.), which, in his opinion, is probably due to the altered relation between albumin and globulin. The latter contributes perhaps in giving the peculiar character to the frozen serum which conditions the variations of the electrolyte which it expands.

FROM THE AUTHOR'S ABSTRACT.

Chronic Infectious Diseases

APPLICATION OF POWDERED POTASSIUM PERMANGANATE TO TUBERCULOUS LESIONS. V. TRIPPUTI, Riv. di clin. pediat. **40**:183 (March) 1942.

A preliminary report is presented of beneficial results from the application of 0.5 Gm. of potassium permanganate in powder form to tuberculous ulcers of the skin and to fistulas resulting from tuberculous lymphadenitis; the application was repeated every five days. The salt acts as a caustic and seems to stimulate the formation of connective tissue.

HIGGINS, Boston.

TUBERCULOUS MENINGITIS IN CHILDREN: REVIEW OF 530 CASES. R. GIUNTINI, Riv. di clin. pediat. **41**:23 (Jan.) 1943.

Five hundred and thirty children with tuberculous meningitis were seen at the pediatric clinic in Florence between 1892 and 1941; 256 autopsies were performed in this series. The disease was commonest in the first two years of life; the incidence was highest in the spring and after epidemics of measles and whooping cough. The source of the infection could be ascertained in about one-half the cases. The disease was most likely to appear shortly after the initial tuberculous infection.

HIGGINS, Boston.

Diseases of Blood, Heart and Blood Vessels and Spleen

CHANGES IN BONE ASSOCIATED WITH LEUKEMIA IN CHILDREN: RHEUMATOID FORMS OF LEUKEMIA. ROBERT F. LANDOLT, Helvet. pædiat. acta **1**:461 (Oct.) 1946.

The skeletal changes associated with infantile leukemia were studied in 48 cases of children who had been under observation during the last ten years in the Zurich Children's Hospital.

Generalized osteoporosis was established in 10 cases; occasionally a more maculated picture was observed.

"Rarefaction lines" (as they are called) were established in 22 cases. These clear, tenioid zones are due to localized osteoporosis with decalcification processes, and the localization at the place of the most pronounced growth with a good vascular supply is of great importance. As the formation of these rarefaction lines requires some time, their early occurrence in leukemia implies that the leukemic process was present long before the appearance of clinical symptoms. The rarefaction zones occur not only in leukemia but also in many other diseases of long duration.

Actual foci of destruction were observed in 11 cases; the "moth-eaten" appearance of the bones is characteristic. In 4 cases pronounced periosteal stripes were observed in addition to the foci of destruction.

A case of acute leukemia in a boy 1 year 2 months of age showed extensive diffuse osteosclerosis.

Of the 48 cases of leukemia, there were osseous changes in 29. If only those cases in which skeletal photographs were made (38) are taken into consideration, the frequency is 76.3 per cent. The skeletal changes are, however, equivocal, and there are none which are absolutely typical for leukemia.

The rheumatoid form of leukemia is particularly well defined clinically. Altogether, 10 cases of this type were observed. Characteristic of this form are the spasmodic pains which occur in all of the joints and neighboring parts, sometimes accompanied with swelling and reddening of the affected parts; aleukemic or subleukemic leukocytic values; lymphoid character in the paraleukoblasts; occasionally a nonspecific exanthem, and a protracted course. It is assumed that in this rheumatoid form of leukemia the defense mechanism of the organism is particularly effective and that some of the symptoms are of a hyperergic-allergic origin. Attention is drawn to the difficulties in the differential diagnosis of this form, and the importance of sternal puncture is emphasized.

FROM THE AUTHOR'S SUMMARY.

VARIATIONS FROM STANDARD HEMATOLOGIC VALUES AS A CONSEQUENCE OF DEFICIENT DIET. S. I. DE VRIES, Nederl. tijdschr. v. geneesk. **90**:1434 (Oct. 19) 1946

The author determined the number of red cells, the hemoglobin content, the serum iron level and the size of the red cells in 100 normal Netherland men and women belonging to various classes of the population. The results were compared with the normal standard values obtained in 1941. The number of red cells and the hemoglobin content had decreased, whereas the mean corpuscular volume, the mean thickness of the red blood corpuscles and the spherical index had increased considerably. These changes were due to a deficient diet.

VAN CREVELD, Amsterdam, The Netherlands.

RELATION OF PIGMENTS WITH A POSITIVE DIAZO REACTION AND PIGMENTS WITH A NONPOSITIVE DIAZO REACTION IN THE SERUM OF ICTERIC PATIENTS. S. LUPS and F. G. D. MEYER, Nederl. tijdschr. v. geneesk. **90**:1445 (Oct. 19) 1946.

In the serum of normal persons the ratio of the pigments which do not give a positive Ehrlich diazo reaction (the carotenoid pigments excepted) and the pigments which give a positive diazo reaction is 0.16 ± 0.08. In cases of epidemic hepatitis and jaundice caused by cholelithiasis, this quotient increases considerably at the height of the jaundice and, especially, as it begins to disappear. In the final phase values as high as 1.00 ± 0.19 (epidemic hepatitis) and 1.04 ± 0.28 (cholelithiasis) are observed, with a normal bilirubin content of the serum.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of Nose, Throat and Ear

RELIEF OF SORE THROAT FROM BISMUTH SUPPOSITORIES CONTAINING A BISMUTH SALT. A. GISMONDI, Riv. di clin. pediat. **40**:171 (March) 1942.

Fifteen persons with sore throat and tonsillitis were treated with suppositories of a bismuth salt in a base containing lecithin. Relief usually occurred in twelve to seventeen hours and the temperature then became normal. If fever persisted, another suppository was inserted. The rectal administration is more acceptable to the patient than the intramuscular injection, as recommended by Montieri. If diphtheria is suspected, diphtheria antitoxin must also be given.

HIGGINS, Boston.

Diseases of Lungs, Pleura and Mediastinum

VOLUNTARY BREATHHOLDING: II. THE RELATION OF THE MAXIMUM TIME OF BREATHHOLDING TO THE OXYGEN TENSION OF THE INSPIRED AIR. GEORGE L. ENGEL, EUGENE B. FERRIS, JOSEPH P. WEBB and CHARLES D. STEVENS, J. Clin. Investigation **25**:729 (Sept.) 1946.

From ground level to altitudes of 16,000 feet (4,800 meters), the maximum time of breath holding varied in direct proportion to the changes in atmospheric pressure (oxygen tension of inspired air). Similar variations were noted on the ground when equivalent gas mixtures were inspired by mask. Breathing mixtures containing from 21 to 100 per cent oxygen progressively increased the breath-holding time, but the effect became progressively less as the oxygen tension approached 760 mm. of mercury. A decrease in breath-holding time occurred at 7,000 feet (2,100 meters) in all persons tested.

FROM THE AUTHORS' SUMMARY.

TRUE DIAPHRAGMATIC HERNIA. L. D. EERLAND, Nederl. tijdschr. v. geneesk. **90**:1450 (Oct. 19) 1946.

The author reports the case of a 12 year old patient with hernia diaphragmatica vera parasternalis. A part of the liver was in the hernial sac. The shadow on the roentgenogram was seen when the patient was 6 months of age. It had the appearance of a teratoma of the anterior mediastinum. The diagnostic possibilities of mediastinal tumor are manifold. Sometimes it is possible to predict with a fair degree of accuracy what will be discovered at thoracotomy. Uncertainty as to the nature of the pathologic process causing a shadow on the roentgenogram can be dispelled only by an exploratory thoracotomy or excision. Even if there are no or few symptoms, this procedure should be carried out. The policy of watchful waiting is to be condemned because of the potential danger of mediastinal cysts and tumors (infection, malignant degeneration).

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE USE OF POTASSIUM CHLORIDE IN THE TREATMENT OF THE DEHYDRATION OF DIARRHEA IN INFANTS. CLIFTON D. GOVAN JR., and DANIEL C. DARROW, J. Pediat. **28**:541 (May) 1946

The recent studies of Darrow have shown that prolonged or intense episodes of diarrhea lead to large losses of potassium, as well as of sodium, chloride and water. The loss of potassium is out of proportion to the loss of nitrogen and, therefore, is an important aspect of the disturbance of the electrolyte pattern

in infants with diarrhea. The administration of potassium can replace this deficit at a time when food cannot be given without aggravating the diarrhea.

To replace these losses of water and electrolyte in severely dehydrated infants, a solution having approximately the following composition per liter was administered intravenously and subcutaneously: potassium, 35 millimols; sodium, 122 millimols; chlorine, 104 millimols; lactate, 53 millimols.

The solution was made according to the following formula, and then antoclaved: potassium chloride, 2 Gm.; sodium chloride, 3 Gm.; sixth-molar solution of sodium lactate, 250 cc., and water, 500 cc.

During the first twenty-four hour period, in addition to the use of whole blood and plasma in the treatment of shock, the potassium chloride–sodium chloride–sodium lactate solution was administered in amounts varying from 70 to 150 cc. per kilogram of body weight. A sufficient amount of 5 per cent solution of dextrose was then given intravenosuly to bring the total fluid intake for the day up to from 200 to 250 cc. per kilogram of body weight. After the first twenty-four hours further losses of water and electrolyte were compensated by the administration of smaller amounts of the potassium chloride–sodium chloride–lactate solution and dextrose.

The parenteral injections of the potassium solution were continued until there was evidence that the dehydration had been overcome and until intestinal absorption appeared normal. When feeding was resumed, a mixture of equal parts of skimmed milk, lactic acid and milk, with the addition of 5 per cent "dextrimaltose" (a preparation of dextrin and maltose) was given.

As the potassium chloride–sodium chloride–sodium lactate mixture contained ten times the amount of potassium found in the extracellular fluids, two precautions were observed. The solution was never administered intravenously more rapidly than at the rate of 2 cc. per minute and usually was not given until evidence of formation of urine was assured. The failure to observe the last precaution resulted in a clearcut instance of potassium intoxication.

The period of observation extended from June to November 1945, during which time 104 infants with diarrhea were admitted to the Harriet Lane Home. From June to September, 53 of these infants received the conventional form of treatment, and 17 died. From September to November, 51 received, in addition to the conventional form of treatment, parenteral injections of the solution of potassium chloride, and only 3 died. Owing to the limited number of beds, only severely ill patients were admitted to the wards, and, as a result, the severity of the illness of the infants in both groups was comparable. The ages of the infants were also comparable: At least 80 per cent of the infants in both groups were under 6 months of age.

Of the 3 infants who died in the group receiving parenteral injections of the solution of the potassium salt, 1 was a 25 day old infant who had had diarrhea for twenty-three days; another was an infant who died six hours after admission, and the last was a patient with congenital syphilis who had had no diarrheal stools for five days before death and, although he had two loose stools the night he died, diarrhea would not ordinarily be considered the cause of death. Of the first 43 infants treated with parenteral injections of potassium, only 1 did not live. These infants survived the month of September, when the rate of mortality from diarrhea in Baltimore is usually quite high.

The plan of treatment described apparently did not shorten the period of the watery diarrhea. However, the infants looked better in a shorter time after this form of therapy was instituted and were able to survive a period of diarrhea that otherwise would have been fatal.

AUTHORS' ABSTRACT.

ENTEROGENOUS CYST OF THE ILEOCECAL REGION. W. HARRISON MEHN and WILLIAM J. MORROW, J. Pediat. **28**:605 (May) 1946.

Enterogenous developmental cysts of the ileocecal region are rare. Fifty-two cases have previously been reported, most of them of infants and children. Cysts may occur anywhere along the alimentary tract, from the base of the tongue to the rectum, but the commonest site is the ileocecal region. Enteric cysts arise from and reproduce the structure of the normal intestinal wall. They are usually attached at the mesenteric border. The cavity of the cyst is unconnected with the lumen of the bowel and contains mucus. The origin of such cysts may be from remnants of the vitelline duct; they may develop from buds of endothelial tissue pinched off the primitive gut, or they may arise from an abnormal persistence of vacuoles present in the solid stage of intestinal development.

The cysts may produce obstruction, pain and bleeding. Acute obstruction is the commonest condition. The symptoms may simulate acute intussusception, acute appendicitis or appendical abscess. There may be a palpable, freely movable abdominal tumor. Diagnosis is usually made only at operation or autopsy. Roentgenographic examination may or may not show a filling defect in the region of the ileocecal valve.

Treatment consists in resection and anastomosis, with or without a safety valve ileostomy above the anastomosis; enucleation of the cyst, evacuation of the cyst, with or without permanent drainage; marsupialization of the cyst, and by-passing the region of the cyst with an enterocolostomy. Resection and marsupialization are the procedures of choice. Adequate postoperative care, in the form of decompression and parenteral administration of fluids, blood and serum, is of great importance.

A 14 day old boy was seen because of hiccups, vomiting and bloody stools. The baby had lost weight from birth and had regurgitated his feedings in the nursery. Two bloody stools preceded his admission to the hospital. Examination revealed epigastric waves and a firm, movable, slightly tender, mass, measuring 3 cm., in the right lower quadrant of the abdomen. Rectal examination revealed blood. A preoperative diagnosis of atypical intussusception was made.

At operation a 2.5 cm. mass was observed within the lumen of the terminal portion of the ileum. The cecum, appendix and terminal part of the ileum were resected, and an end to side ileocolostomy was performed. Postoperative care included decompression and parenteral administration of serum, blood and fluids. On the fifth postoperative day it was possible to feed the infant orally, and the subsequent course was uneventful.

The pathologic report was that of an obstructing cyst 2 cm. in diameter lying in the terminal portion of the ileum and attached at the mesenteric border. The cavity of the cyst contained mucus and was unconnected with the lumen of the bowel. The cystic wall was composed of smooth muscle fibers and connective tissue and was lined on both sides with intestinal epithelium resembling that of the terminal portion of the ileum.

The clinical, surgical and pathologic observations in the case are similar to those described by previous authors.

AUTHORS' ABSTRACT.

VOMITING IN INFANTS AND HYPERTROPHY OF THYMUS. ALESSANDRO ZANINI, Pediatria **54**:290, 1946.

The author, after presenting the cases of several sucklings affected by vomiting and slight hypertrophy of the thymus, discusses the success of the use of roentgen therapy and considers the relation of hyperfunction of the thymus and vomiting.

FROM THE AUTHOR'S SUMMARY.

GANGRENOUS STOMATITIS CURED WITH PENICILLIN: REPORT OF A CASE. ARMANDO CARNEVALE, Pediatria **54**:303, 1946.

The author presents a case of severe noma in a girl 3 years of age who recovered after treatment with penicillin. He ascribes the therapeutic success not only to use of this powerful antibiotic but to the other measures employed (blood transfusions, administration of vitamin A and ascorbic acid), which stimulated the general organic defenses and guarded against eventual deficiency states.

FROM THE AUTHOR'S SUMMARY.

GLYCOGENOSIS ON (VON GIERKE'S DISEASE). A. CHIEFI and L. NASSI, Riv. di clin. pediat. **39**:623 (Dec.) 1941.

Studies were made on 3 patients with glycogenosis. Observations on the blood sugar curves were made after the patient had received various vitamins (thiamine, riboflavin, pyridoxine and pantothenic acid) and hormones (extracts of the anterior and posterior lobes of the pituitary, desoxycorticosterone and the fat-soluble extract of the thymus). Pyridoxine and adrenal cortex extract caused definite elevations of the blood sugar curve. Injections of epinephrine did not cause the rise in blood sugar usually seen in normal children and, on one occasion, produced a striking fall in the blood pressure.

HIGGINS, BOSTON.

MIKULICZ' DISEASE. JOSÉ CELORIA and JORGE A. GÜEGLIO, Rev. Soc. pediat. d. litoral **10**:253 (Sept.-Dec.) 1945.

The case of a 12 year old girl is presented by the authors. Only the parotid and submaxillary glands were affected; there was no involvement of the lacrimal glands. Biopsy revealed lymphoid infiltration. The authors discuss the differential diagnosis of swellings of the salivary glands and present the various theories of the cause of Mikulicz' disease. The condition occurs mostly in persons between 20 and 30 years of age; children are rarely affected.

SOLMITZ, Chicago.

BOECK'S SARCOID (GENERALIZED SARCOIDOSIS) WITH INVOLVEMENT OF SALIVARY GLANDS: REPORT OF A CASE. HANS ZELLWEGER, Helvet. pædiat. acta **1**:485 (Oct.) 1946.

The author reports a case of sarcoidosis (Boeck's sarcoid), verified by biopsy, with generalized swelling of the salivary glands, enlargement of the epididymis, hepatosplenomegaly, pseudoleukemia (polyadenia), typical changes of the oral mucous membrane and rhinitis sicca, the last previously unknown in a case of sarcoidosis. In addition, a decrease in production of pancreatic ferments and disturbances of carbohydrate metabolism, caused by the deficient secretion of the salivary glands, were observed. Oral and intravenous "loading" with dextrose gave low loading curves with only a slight epinephrine effect. After injection of epinephrine there was a slight rise, and after the injection of insulin a fairly definite fall, in the blood sugar level. Some authors ascribe an anti-insulin effect to the secretion of the salivary glands, while others say that its action is identical with that of insulin. To explain this paradox, the following hypothesis has been postulated: The secretion of the salivary gland slows down the rate of combustion of sugar at the periphery and thus has an anti-insulin effect in so far as it prolongs alimentary hyperglycemia.

FROM THE AUTHOR'S SUMMARY.

Psychology and Psychiatry

A MENTAL EPISODE IN A PSYCHOPATHIC CHILD. NELIDA B. DE VITA and A. VITA, Rev. Soc. pediat. d. litoral **10**:239 (Sept.-Dec.) 1945.

A boy 11 years of age, coming from a family with psychopathic tendencies, exhibited abnormal personality traits as early as the age of 5 years: mental precocity, irritability, laziness, tendency to vagabondage, nightmares and excessive masturbation. He did not make friends, showed no affection toward members of the family and was indifferent to his surroundings. At the age of 11, an acute schizophrenic episode occurred: This began with sudden periods of extreme fear, in which he felt that he was choking or was going to die, so that he cried for help. Later he was troubled with strange sensations in various parts of his body; his hands and feet felt as though they did not belong to him, and food tasted strange. Sometimes he believed he was dead and was among corpses. He did not recognize persons he knew well; on the other hand, he believed that he knew persons who were perfect strangers. During this time he lived as though in a dream although troubled by a sense of anxiety and despair. He was hospitalized, and the episode cleared up within three months.

According to the authors, this case is interesting for two reasons: (1) the occurrence of a true schizophrenic episode in a neuropathic child at the early age of 11 years, and (2) the importance and success of psychotherapy in this case. The authors believe that the development of later schizophrenic episodes in such cases can be prevented if the modern psychotherapeutic methods (persuasion therapy and the Sakel treatment) are applied early. The younger the patient, the greater is the mental plasticity and the beneficial effect of proper educational and environmental factors. If possible, treatment should start before the age of 6 years.

SOLMITZ, Chicago.

Diseases of the Genitourinary Tract

ALBUMINURIA, ARTERIAL PRESSURE AND BODY BUILD OF SCHOOL CHILDREN AS AFFECTED BY THEIR POSTURE. C. PESCATORI, Riv. di clin. pediat. **40**:228 (April) 1942.

Examinations of the urine and the blood pressure of 50 school children 7 to 13 years of age were made both before and after a three hour school session in Parma, Italy. When the children were kept at attention without rest periods, albuminuria developed in 12, or 24 per cent, although in none was the condition present before the school session. When ten minutes of physical exercise and relaxation were allowed the children each hour, none of the children had albuminuria. After the three hour period without rest, the children with a relatively high initial pressure showed a lower blood pressure, and the children with a low initial blood pressure showed a rise. When there was a recreation period each hour, these changes were not observed. The body build of the child had no relation to the albuminuria.

HIGGINS, Boston.

Diseases of the Ductless Glands; Endocrinology

NATURE OF CIRCULATING ESTROGEN: LIPOPROTEIN-BOUND ESTROGEN IN HUMAN PLASMA. SIDNEY ROBERTS and CLARA M. SZEGO, Endocrinology **39**:183 (Sept.) 1946.

The data reported strongly suggest the existence of a specific protein-estrogen complex in human blood. The protein component of this estroprotein is probably

of the beta-globulin type, since it fractionates into fraction III-O of Cohn. Evidence is presented that the estrogen component of this complex is probably mainly estriol.

JACOBSON, Buffalo.

ADRENAL FUNCTION IN PREGNANCY. ELEANOR H. VENNING, Endocrinology **39**:203 (Sept.) 1946.

The important contributions made in recent years with regard to the metabolic changes produced by the adrenal cortex steroids show that the various functions of the adrenal glands, such as salt and water metabolism, carbohydrate and protein metabolism and androgenic activity, can be correlated with different groups of steroid hormones. Evidence is accumulating to indicate that these various functions may exert their influence independently of one another. The present research on the excretion of adrenal metabolites in pregnancy suggests that at least the corticoids, those compounds of adrenal origin which have a specific effect on carbohydrate and protein metabolism, and the 17-ketosteroids can vary independently of one another

In the present series of pregnant women, a definite increase in excretion of corticoids was observed, with little change in the 17-ketosteroids.

JACOBSON, Buffalo.

Diseases of the Muscles, Bones, Joints and Lymph Glands

HODGKIN'S DISEASE IN CHILDREN. HERMAN CHARACHE, New York State J. Med. **46**:507 (March 1) 1946.

Hodgkin's disease is comparatively rare in children. At the time this article was written, 233 cases had been recorded in the literature. The author adds 11 additional cases from the Brooklyn Cancer Institute, briefly reviews the literature and includes a complete bibliography on the subject. The symptoms, diagnosis, treatment and prognosis are discussed.

Even to a greater degree than in adults, the disease in children is commoner in males than in females (82.7 to 17.3 per cent). Eight of the recorded cases were of infants between the ages of 2 and 5 months. Hodgkin's disease in Negro children is rare. If tuberculosis is a precursor of the disease, the reverse should be true, since tuberculosis is more prevalent in that race.

A swelling of the neck is usually the first symptom, and the left cervical glands are more frequently involved. It is believed that all cases begin with abdominal involvement and that the disease then spreads to the other lymph nodes. Mediastinal involvement is commoner in children than in adults, whereas the reverse is true of cutaneous manifestations. The blood picture is not diagnostic.

The only positive basis for diagnosis is the histologic study of an excised gland. The treatment of choice is radiation.

The prognosis for children is poor, and even graver than for adults. The average duration of the disease in the recorded cases was approximately two years.

AIKMAN, Rochester, N. Y.

Society Transactions

AMERICAN ACADEMY OF PEDIATRICS

J. I. Durand, M.D., *President*

National Meeting, Pittsburgh, Feb. 24-27, 1947

ROUND TABLE DISCUSSION

VI. Diseases of the Nose and Throat

Joseph Yampolsky, M.D., Atlanta, Ga., *Secretary*

R. H. Graham, M.D., Aurora, Ill., *Secretary*

Chemotherapy and Use of Antibiotics in Combating Aural Suppuration.
DR. STANTON A. FRIEDBERG, Chicago.

The use of chemotherapeutic measures for combating severe infections came into prominence in this country about ten years ago. With the rapid progress being made in the development of new antibacterial agents, another ten years may again alter one's concepts as decidedly as they have been in the past decade. Since there have been striking revisions in the knowledge and methods of treatment of acute and chronic middle ear suppuration, as well as in views on changes in the middle ear due to obstruction of the eustachian tube, an evaluation seems in order. This report on present day problems of pediatric otology is concerned particularly with suppurative processes. The corollary subject of hearing impairment in children will be presented by Dr. John E. Bordley.

A brief review of certain practical anatomic considerations is important. It is necessary to recall that mesenchymal tissue fills the middle ear cavity during fetal life and at birth and that a close relation exists between its disappearance and the onset of pneumatization of the mastoid process. Any local inflammatory process may impede the normal resorption of mesenchymal tissue from the middle ear and arrest pneumatization, causing permanent hypertrophy of the submucosa of the tympanum and lack of development of the mastoid process. It is also to be remembered that in the infant the angle of inclination of the tympanic membrane is much greater than it is in the adult, and corresponding precautions are necessary in incising the drum. Another significant factor is the relative thickness of the infant tympanic membrane, requiring more intratympanic pressure for spontaneous rupture. Hence, it is not uncommon to observe a subperiosteal abscess in an infant even before any aural drainage is evident.

Pneumatization of the mastoid bone proceeds from the mastoid antrum, which is the lone cell present at birth. Normal development is later represented by the "pneumatic mastoid." Partial arrest of the process is seen in the diploic type of mastoid, while completely arrested development is evidenced by a sclerotic type of bone. In such cases there is often a striking difference in the actual size of the mastoid process on the normal and on the involved side in the same person. The roentgenogram thus offers considerable chronologic information in the important differentiation between a primary acute condition and an acute exacerbation of a more chronic infection.

The eustachian tube in infants and children is known to be more horizontal, relatively wider and shorter than it is in adults, with the result that the middle ear is more susceptible to infection from adjacent structures. The facial nerve is superficial; dehiscences are common, and bony protection as the nerve leaves the skull is frequently lacking for twelve to eighteen months. Thus, extra care in instrumental delivery and in surgical procedures on the mastoid is of extreme importance. Finally, it should be pointed out that the dura of the middle cranial fossa connects with the middle ear via bony processes, and occasionally by blood and lymph vessels. Thus, dural hyperemia and irritation, manifest as "meningismus," may result from inflammation of the middle ear.

ACUTE SUPPURATIVE OTITIS MEDIA AND MASTOIDITIS

It is unnecessary to extol the advantages of chemotherapy and the use of antibiotics in the management of acute suppurative otitis media. Surveys from large institutions portray the diminishing morbidity span of the disease and the decreasing incidence of acute mastoiditis. Figures from the Royal Infirmary at Edinburgh show a 35 per cent incidence of mastoid complications in 1932, contrasting with a 9 per cent rate in 1941 (Adams, W. S., and Martin, G. E.: Use and Misuse of Sulfonamides in Otitis Media, *J. Laryng. & Otol.* **59**:297-308 [Aug.] 1944). De Sanctis and Larkin's statistics (Otitis Media and Mastoiditis in Children, *J. A. M. A.* **120**:1087-1093 [Dec. 5] 1942), covering 1,992 cases, are similar. Falbe-Hansen and Becker-Christensen (On Sulfonamide Therapy in Acute Suppurative Otitis Media, *Acta otolaryng.* **32**:209, 1944) cited an operative percentage of 1.5 in a series of treated patients and of 9.3 per cent in a control group. Otitis complicating scarlet fever, one of the most virulent forms of middle ear suppuration, yields rapidly to penicillin treatment, according to Weinstein and Atherton (The Treatment of Acute Suppurative Otitis Media with Penicillin, *J. A. M. A.* **129**:503-509 [Oct. 13] 1945).

But there is an increasing tendency to rely exclusively on these drugs, often to the neglect of certain basic principles. A tympanic cavity filled with purulent exudate requires surgical drainage by paracentesis. If the exudate is allowed to remain undisturbed, its fibrinous elements will undergo gradual replacement with fibrous tissue, and a permanent adhesive process will be inevitable. Otologists are now seeing many children whose middle ear deafness seems directly traceable to this very phenomenon. The drugs in use are only bacteriostatic. A surgical focus may eventually become sterile, but the cellular elements contained therein are subject to nature's constant healing pattern.

Farquharson (The Masking Effect of Sulfonamides in the Treatment of Acute Otitis Media, *J. Laryng. & Otol.* **60**:269-278 [July] 1945) observed that "in the last eight years appreciable deterioration in hearing has been noticeable in cases of otitis media. . . . This must be put down to the masking effect of the drug causing delayed drainage from the middle ear. . . ." He suggested that this delayed drainage may be due to an adhesive inflammatory process or, as proposed by Kopetsky, a labyrinthine hydrops caused by a chemical reaction between the perilymph behind the oval and round windows and the purulent contents of the middle ear. Obviously, only prompt drainage of the ear will prevent the hearing loss which might result from permanent alterations by either or both of the aforementioned reactions.

Surgical foci, then, must be treated as such. Abscesses in the middle ear require opening, and processes of bone destruction, such as those in coalescent mastoiditis or cholesteatoma, must be eliminated.

It is well recognized that the best results with chemotherapy and allied measures are obtained when surgical indications are heeded, when treatment is begun as early as possible, employing an adequate dosage, and when the particular offending organism has been identified by culture.

By what criteria may the efficacy of treatment of acute suppurative otitis media be measured? Probably the two most important are the temperature readings and the status of the aural discharge. When the ear has stopped draining and the temperature remains normal, all activity may be presumed to have ceased. However, it is extremely important to continue medication for several days after these criteria have been fulfilled. (Slides were shown illustrating the recurrence of fever and aural discharge following premature discontinuance of therapy.) Persistence of fever without drainage, or the converse, must be regarded with suspicion.

How long is one justified in continuing therapy? If chemotherapy or treatment with penicillin has not controlled an acute infection of the middle ear in seven to nine days, provided that adequate blood levels have been maintained, the medication should be stopped. Beyond this point, one must study the patient for signs of a process no longer limited to the middle ear. Furthermore, a drug reaction, though less common with the newer sulfonamide derivatives than formerly, is most apt to occur at about this time. Fever, chills and headache appearing during the course of otitis media offer a perplexing problem of differential diagnosis between the development of a new focus of infection and a drug reaction. On such occasions every otologist has had the experience of wishfully recalling the days when the significance of such a response by the patient was indeed clearcut in its implications.

There is still another problem which occasionally confronts one, namely, the complete failure of therapy. Certain strains of bacteria simply do not respond. Several instances can be recalled in which, despite cultures, adequate blood levels and optimal conditions for observation, coalescent mastoiditis appeared in thirteen to eighteen days and required surgical intervention. Procrastination in a case of this type of infection is unwarranted. In this connection, it should be mentioned that the successful use of penicillin has recently been reported in the treatment of certain sulfadiazine-resistant strains of hemolytic streptococci (Allman, C. H.: Penicillin in Otology, *J. A. M. A.* **129**:109-112 [Sept. 8] 1945). The testing of species sensitivity in vitro should be carried out before the institution of random trial therapy in refractory cases.

What of the patient who, when first seen, presents the history, symptoms and signs of acute mastoiditis and, perhaps, has received a previous inadequate course of therapy? (It is rare in these times to encounter a patient with otitis media who has not received the little white pills every four to six hours for at least several days.) There certainly can be no objection to instituting chemotherapy or the administration of penicillin providing the basic pathologic process is recognized and one remains alert to the probable necessity of surgical intervention if the desired improvement is not immediately apparent. Any prolonged continuation of conservative treatment, however, is not justified in the presence of outright indications for operation. It may, in fact, be extremely hazardous. (Slides were shown illustrating the masking of sinus thrombosis by sulfonamide drugs.) Here, again, it is essential to recall that the roentgenogram is frequently altered by the action of the drugs now employed.

The local use of sulfonamide compounds and antibiotics is of no value in cases of acute otitis media. Nevertheless, there are practitioners who advocate administration in this form as a supplement to surgical measures, especially in the postoperative care of mastoidectomy wounds. Whether there are any benefits resulting

which cannot be achieved with systemic administration is a controversial issue at present.

It is important that various adjuncts to treatment be employed. Any concomitant sinusitis or nasopharyngeal infection must be diligently sought and cared for. Again, it must be emphasized that the agents now in use are bacteriostatic rather than bactericidal, and one must bear in mind that, in the last analysis, the patient must build up his own immunity in order to overcome infection. Accurate cultures will be helpful in supplying knowledge as to type-specific serums which might be used, particularly with the pneumococcic infections of children. Anemias must be corrected by appropriate measures, and, not infrequently, small transfusions will provide the necessary aid to a favorable outcome.

CHRONIC SUPPURATIVE OTITIS MEDIA

A consideration of this subject requires elucidation of the causes and types of infection encountered.

Chronic otitis media oftenest occurs as a sequel to the severe necrotizing inflammatory process which accompanies scarlet fever or measles. Chronicity may also follow ordinary acute otitis media in an ear in which the mucosa is hyperplastic as a result of an earlier inflammatory condition, predisposing to lack of normal healing capacity. Finally, there may be cholesteatoma formation, either as a result of prolonged negative pressure in the middle ear or by virtue of nature's attempt to heal a marginal defect in the tympanic membrane.

An anterior inferior defect in the tympanic membrane is usually spoken of as a tubal perforation. More commonly seen is the central perforation. Epitympanic (or attic) defects and marginal perforations are most frequently characterized by cholesteatoma formation.

It is well to bear in mind these pathologic processes and their relation to vital structures, particularly in relation to cholesteatoma and carious disease of neighboring bony structures.

Central and tubal perforations are usually benign, requiring only local measures and attention to sinal or nasopharyngeal pathologic conditions for the control of the discharge, which recurs periodically. This secretion, incidentally, is predominantly mucoid and nonodorous. The persistent odorous discharge accompanying cholesteatoma or osteitis, however, is a warning signal that should be heeded. As long as it continues unchecked, there is a real danger of extension of the process to the labyrinth, the dura of the middle cranial fossa, the facial nerve, the lateral sinus or the cerebellum.

Results of attempts to control the progress of this type of chronic suppuration with chemotherapy and treatment with antibiotics have been universally disappointing, and it is the injudicious persistence in this practice which has caused considerable alarm of late. For, despite the decreasing incidence of complications of acute disease of the middle ear, the percentage of aural intracranial complications has not altered; if anything, it has been a little higher in recent years (Adams and Martin, previously cited). Estimates of the death rate from complications show that it has remained the same, or has increased over previous years. These figures are particularly significant when viewed in relation to the over-all drop in the actual number of complications. To quote again from Farquharson:

"It is a matter for profound meditation that the drug which has produced such miracles in the treatment of otitic meningitis is the same drug which, used misguidedly, is indirectly responsible for the development of the disease itself; by masking symptoms that would have indicated surgical intervention."

Current interest in streptomycin necessitates a word of caution regarding its use. Toxic reactions affecting the vestibular apparatus occur in a high percentage of patients who receive the drug over a period of three weeks or more. So far as is known at present, the resulting depression of labyrinthine function is permanent (Brown, H. A., and Hinshaw, H. C.: Labyrinthitis Following Streptomycin Therapy, *Proc. Staff Meet., Mayo Clin.* **21**:347-352 [Sept.] 1946). Auditory loss, though less common and less severe, seems to follow the same pattern. The value of streptomycin is not to be doubted, but its random use should certainly be discouraged.

SUMMARY

The value of chemotherapy and antibiotics in combating acute suppurative aural disease is well established. Reliance on these agents to the exclusion of basic principles of surgical drainage may lead to irreversible adhesive processes in the middle ear and to the masking of serious complications. Control with chemotherapy of chronic suppurative otitis involving bone has been disappointing, and the mortality rates from sequelae of this condition have not changed significantly in recent years. The importance of an understanding of fundamental pathologic factors, of judiciously planned treatment and of timely operative measures is now even more apparent than before the advent of the newer therapeutics.

The Nasopharynx. DR. JOHN E. BORDLEY, Baltimore.

The simplest and one of the best descriptions of the nasopharynx is to be found in Gray's "Anatomy." It will be of interest, in opening this discussion, to quote it in its entirety (Gray, H.: Anatomy of the Human Body, ed. 20, Philadelphia, Lea & Febiger, 1918):

"The nasopharynx lies behind the nose and above the level of the soft palate: it differs from the oral and laryngeal parts of the pharynx in that its cavity always remains patent. In front, it communicates through the choanae with the nasal cavities and sinuses. In its lateral wall is the pharyngeal ostium of the auditory tube. Behind the ostium of the auditory tube is a recess, the fossa of Rosenmüller. In the posterior wall is a prominence, best marked in childhood, produced by a mass of lymphoid tissue, which is known as the pharyngeal tonsil (or the adenoids)." (Fig. 1.)

The air inhaled and exhaled through the nose must pass through this cavity. The posterior nasal sinuses and the mucous membranes lining the posterior half of the nose drain into the nasopharynx. It is from the nasopharynx that air enters the eustachian tube to equalize the pressure in the middle ear with that of the surrounding atmosphere (fig. 2). In this location, the nasopharynx is the haven of many types of bacterial flora. When the patency of this cavity is interrupted. complications more serious than mere mouth breathing ensue.

The presence of adenoid or lymphoid tissue, which Gray describes as the pharyngeal tonsil, is by far the most frequent cause of malfunction of the nasopharynx. This tissue arises in embryo from Waldeyer's tonsillar ring, which later differentiates into the pharyngeal, faucial and lingual tonsils. Although the greatest mass lies in the midline, lymphoid tissue can be observed in the mucous membranes covering the whole of the posterior and lateral walls of the nasopharynx. In childhood its growth can easily be stimulated by infection. Rapid hypertrophy of small masses of adenoid tissue has been frequently observed by every pediatrician in children with recent acute infection of the upper air passages. Such hypertrophy is brought about by the rapid mitosis of the lymphoid cells lying within the germinal centers scattered throughout the adenoid tissue (fig. 3).

Surgical removal of a large central mass of adenoid tissue may relieve mouth breathing but temporarily if infections recur to stimulate growth of the remaining lymphoid tissue in the mucous membranes. In general, when secondary hypertrophy occurs, adenoid tissue reappears more widely spread on the posterior wall of the nasopharynx than before operation. This process will take place time after time, in spite of surgical intervention, in certain children with frequent infections.

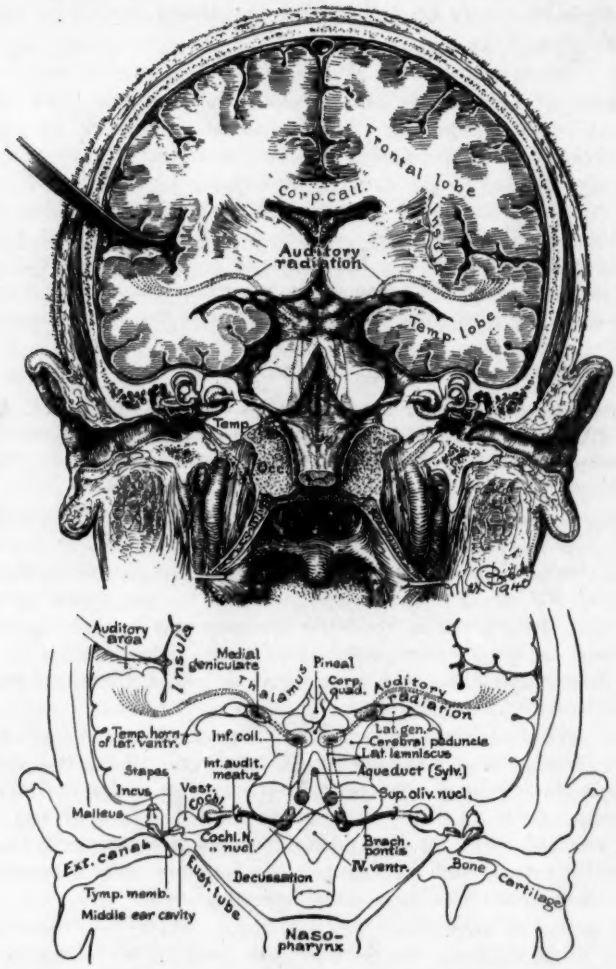

Fig. 1.—Section through the head, showing the anatomic relation of the nasopharynx to its surrounding structures (from Brödel, Max: Anatomy of the Organ of Hearing, in Bothman, Lewis, and others, editors, 1940 Year Book of Eye, Ear, Nose and Throat, Chicago, The Year Book Publishers, Inc., 1940).

At about puberty the activity of the germinal centers of most children tends to slow down, or even to cease, leading in many cases to gradual atrophy of the adenoid tissue present, unless such tissue has become chronically infected as a result of frequent bacterial invasion.

The simplest complication of adenoid hypertrophy is mouth breathing. The mouth breather is a common problem with every physician. The child is a poor feeder and is subject to frequent infections of the upper respiratory tract. As time goes on, a high palatal arch, narrow upper jaw and protruding front teeth develop. His colds frequently result in bronchitis and transient sinusitis, and all too often the pediatrician is called to examine the child because otitis media has developed. The mechanism of such a picture is simple. The obstructing lymphoid tissue has dammed the nasal secretions into the posterior nares, bathing the posterior ethmoid cells and the sphenoid sinuses with infected discharge. The eustachian tubes become closed by the swelling of the mucous membranes, which have become inflamed at the orifices. Mucous secretions are forced back into the middle ear,

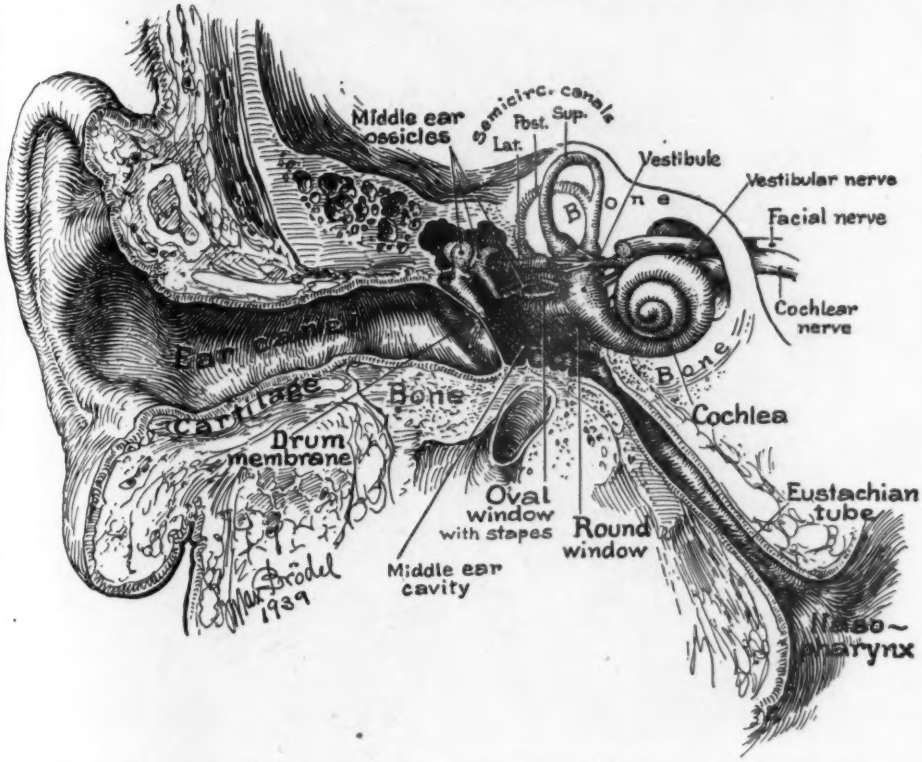

Fig. 2.—The middle ear and eustachian tube (from Brödel, Max: Three Unpublished Drawings of the Anatomy of the Human Ear, Philadelphia, W. B. Saunders Company).

and catarrhal or acute otitis media develops. Without infection, aero-otitis-media may develop in the presence of lymphoid obstruction of the eustachian tube. This condition is due to a negative pressure created in the middle ear when the air in that cavity is absorbed by the lining membrane.

The hypertrophied mass of adenoid tissue itself acts as a splendid incubator for pathogenic organisms; there they may multiply in the mucus-bathed crypts, surrounded with cellular debris. Thus, an infection can be harbored at the top of the upper respiratory tract and the postnasal discharge points toward the trachea and

the bronchial tree. It is this "leaky roof" that so often results in the "wet cellar" of bronchitis in children after a common cold.

Large masses of adenoid tissue in the nasopharynx are easily recognizable and the proper measures for their removal can be instituted early. There is a group of children, however, in whom infected tissue in the nasopharynx may go unrecognized until it has caused permanent damage. These children are not mouth breathers, and frequently they have had an adenoidectomy. In this group the hyperplasia of the lymphoid tissue has become widespread, covering the whole posterior pharyngeal wall, filling the fossa of Rosenmüller and growing over and into the eustachian orifices. It has not, however, closed the nasopharyngeal cavity. The

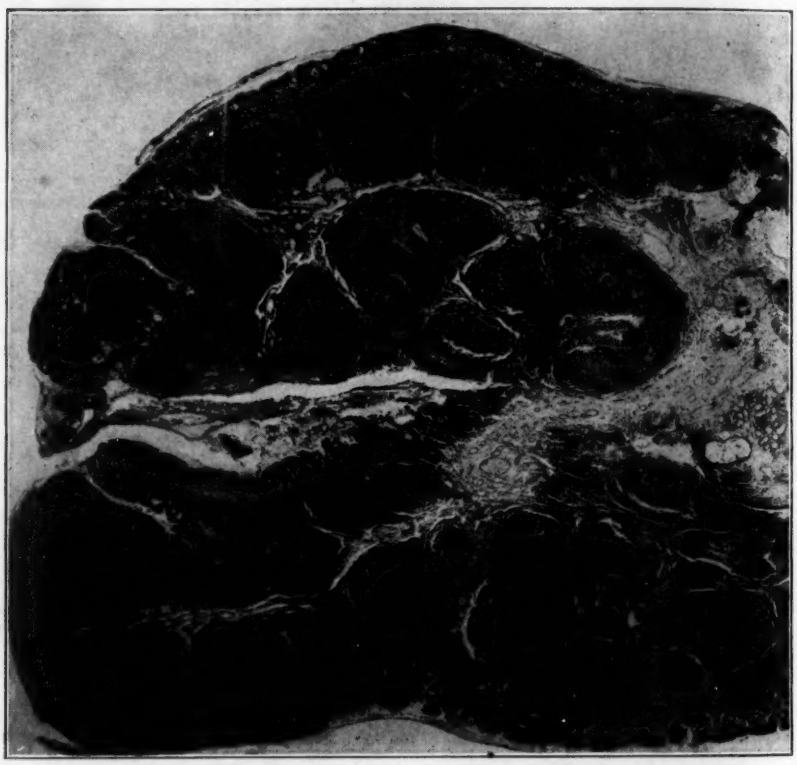

Fig. 3.—Low power photomicrograph of a section through adenoid tissue, showing the germinal centers.

only warning of such involvement a physician may have is transient slight loss of hearing during and shortly after a cold and a pronounced tendency to frequent and protracted colds, often accompanied with bronchitis. Examination of the tympanic membranes of these children while the hearing is impaired will show evidence of retraction, slight injection and often a fluid level, or the chicken-wire appearance of mucous bubbles on the inner surface of the drum. The diagnosis can be confirmed by examination with the nasopharyngoscope (fig. 4).

This condition is subtle and may be overlooked until repeated infections have caused changes in the tissue of the middle ear, resulting in scar tissue. Such tissue will eventually interfere with the normal movement of the ossicles and cause

conduction deafness. The deafness, except during colds, may progress so slowly that the child is considered inattentive, or even mentally slow. Often speech defects are noticeable as the child grows older. If allowed to continue, these changes become irreversible, and the deafness is permanent.

In such cases surgical intervention is not sufficient, as the lymphoid tissue cannot be removed from the lateral walls of the nasopharynx or from the eustachian orifices without endangering the patency of the tube. To shrink the infected tissue

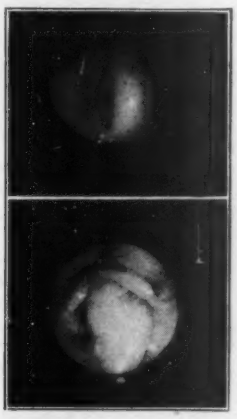

Fig. 4.—Photographs taken through the nasopharyngoscope, showing (above) a normal eustachian orifice and (below) the eustachian orifice overgrown with hypertrophied lymphoid tissue (from Hendricks, J. E., and Lieberman, A. T.: Use of Radium in Aerotitis Control Program of Army Air Forces; Activities of the Irradiation Clinic at Westover Field, Mass., Ann. Otol., Rhin. & Laryng. **54**:668, 1945).

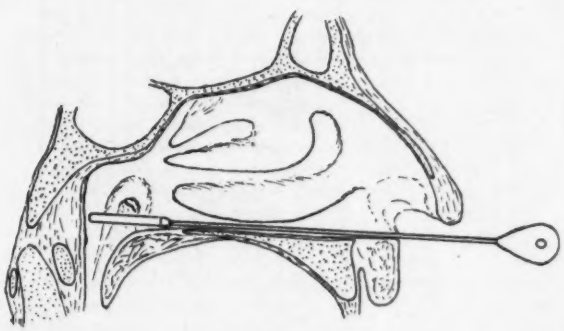

Fig. 5.—The radium applicator shown in place opposite the eustachian orifice (from Crowe, S. J.: Irradiation Treatment of Hyperplastic Lymphoid Tissue in the Nasopharynx, in Jackson, C., and Jackson, C. L.: Diseases of the Nose, Throat and Ear, Including Bronchoscopy and Esophagoscopy, Philadelphia, W. B. Saunders Company, 1945).

around the tubes and on each side of the base of the septum, irradiation is now employed. The easiest and safest form of irradiation is with the use of an applicator containing radium salts or radon gas. Such an applicator may be passed into the nasopharynx through the nose and placed in close proximity to the tissue to be destroyed (fig. 5). With this method, it is not necessary to pass rays through

surrounding structures in order to reach the area to be treated. The irradiation necessary to shrink the lymphoid tissue is so small as to be harmless to the surrounding tissues. Heineke (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **14**:21, 1905) showed that lymphoid tissue is extremely sensitive to irradiation. The applicator now in use gives off a mixture of beta and gamma rays; only the rays absorbed by the germinal cells play any part in the inhibition of mitosis. Thus, as the mature lymphocytes die and are discarded they are not replaced by new cells. This process gradually shrinks the mass of the adenoid tissue. This technic was first employed

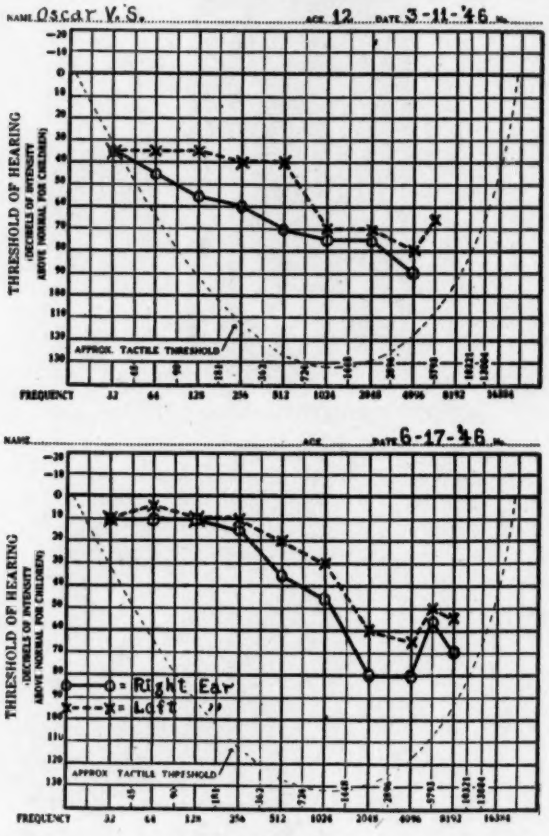

Fig. 6.—Audiograms showing hearing ability of the child with a congenital nerve deafness before and after relief of obstruction of the eustachian tube (from Brodley, J. E.: Use of Radium in the Treatment of Conductive Deafness, Surg., Gynec. & Obst. **84**:839-844, 1947).

by Crowe and Burnam in the otologic clinic of the Johns Hopkins Hospital in 1924 (*Ann. Otol., Rhin. & Laryng.* **50**:15, 1941). During the first decade, before this method was employed freely, almost 100 children were irradiated and closely studied to determine whether there were any untoward effects. In the past ten years more than 25,000 such treatments have been given to children and adults, without complications other than mild coryza. Such irradiation should be combined with surgical measures if the central adenoid mass is large. It may be

necessary to repeat the series of irradiations several times before sufficient shrinkage of the tissue to relieve the symptoms has taken place.

Two interesting cases of children with widespread hypertrophy of adenoid tissue occurred in the Otological Research Laboratory, the Johns Hopkins University School of Medicine. The first child had what appeared to be deafness secondary to obstruction of the eustachian tube (fig. 6). When irradiation relieved that obstruction, the subsequent audiogram showed a typical curve of congenital nerve deafness. It will be noted how the interference in ossicular movement superimposed a conduction loss on this child's congenital lesion and changed the characteristics of the audiogram.

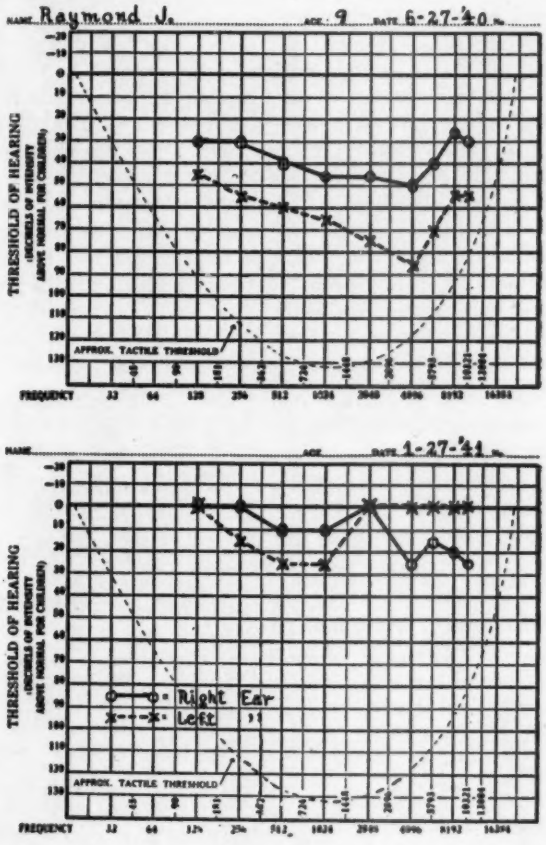

Fig. 7.—Audiograms of the twin boy with defective hearing before and after relief from obstruction of the orifices of the eustachian tubes (from Bordley, J. E.: Use of Radium in the Treatment of Conductive Deafness, Surg., Gynec. & Obst. 84:839-844, 1947).

The second case is interesting from several points of view. The child was one of twin boys. The brother had no evidence of any impediment and stood at the top of the first division of his class in school. The patient was in the second division of the same class; he had a definite speech defect and was reported by the teachers to be inattentive, rather belligerent and possibly slightly retarded. He had had a tonsillectomy and adenoidectomy and gave no history of otitis media or

otalgia. He had been having increasing difficulty in school for two years (fig. 7). An audiogram showed a pronounced hearing loss of conduction type on each side. The tympanic membranes were thickened and severely retracted. The nasopharyngoscopic examination revealed a moderate mass of adenoid tissue in the nasopharynx, completely overgrowing the orifices of the eustachian tubes. An adenoidectomy did not help the hearing, but after irradiation his hearing began to improve and by the middle of the following winter he was having no difficulty with conversation. In two years his speech defect had disappeared and he was ahead of his twin in the first division. In this case the deafness was so insidious that it was missed, and the child's difficulties were attributed to other causes.

In conclusion, it should be emphasized that the nasopharynx, owing to its anatomic position is of the greatest importance to both the ears and the respiratory tract. Its role in infection may affect the sinuses, the ears and the hearing, as well as the bronchial tree. In its lymphoid tissue may be harbored infections which are not always evident, but which influence the proper function of other organs. The role of the lymphoid tissue is especially important before puberty, when the ability to replace itself is at its height. The nasopharynx should be regularly examined and every effort made to keep it clear of infected lymphoid tissue until such an age is reached that the germinal centers are less responsive to the stimulation of infection. Many times tonsils are removed with little attention being paid to the nasopharynx. It should be remembered that the adenoids are much oftener offenders in impairment of the child's health. Tonsils should not be removed except for good and evident cause.

DISCUSSION ON PAPERS OF DR. FRIEDBERG AND DR. BORDLEY

DR. C. H. WEBB, Shreveport, La.: Would you combine sulfonamide drugs and penicillin in the treatment of otitis media?

DR. S. A. FRIEDBERG, Chicago: At present it seems that there is little to be gained by the combined use of penicillin and the sulfonamide compounds in the average case of acute otitis media. Let me again emphasize that not every patient with acute otitis requires chemotherapy and that before these drugs were available the majority of patients recovered without sequelae.

DR. MARYELDA ROCKWELL, Clinton, Iowa: What is your attitude toward oral penicillin, and which form of penicillin do you use?

DR. J. E. BORDLEY, Baltimore: Not enough experience is yet at hand for a comparison of the effectiveness of penicillin given orally with its proved value when given parenterally in cases of acute otitis media.

DR. HUGHES KENNEDY JR., Birmingham, Ala.: Do you use ice water in treatment of hyperemia?

DR. S. A. FRIEDBERG, Chicago: No. The increased blood supply in an area of hyperemia has always seemed to me to enhance leukocytic activity of both defensive and reparative value. I see no reason to discourage the blood supply by the use of ice water, although it appears that the concepts regarding refrigeration are being considerably altered of late.

DR. LOUIS SPEKTER, Hartford, Conn.: How do you detect early hearing loss in a patient with otitis media? This would seem to present special difficulties, inasmuch as the general practitioner often sees the patient first and the pediatrician cannot use the audiometer.

DR. J. E. BORDLEY, Baltimore: The whisper and conversational voice tests are easily carried out on children and are of great value. The physician should resort

to the use of residual air in order to standardize the sounds he produces. The opposite ear may be masked by simply rubbing the palm of the hand across the auricle and external auditory canal.

DR. J. C. SAVAGE, Glendale, Calif.: What about the use of suction?

DR. S. A. FRIEDBERG, Chicago: For office use, spot suction is an excellent aid in the rapid cleansing of the passages of accumulated aural or nasal discharge. It should be done with extreme gentleness. Any mass suction with the nasopharynx occluded will cause considerable trauma to the tissues and is to be condemned. In the home, mild suction with a small bulb syringe or a catheter may be of value in relieving mechanical nasal obstruction due to excessive secretions, particularly when the child is unable to blow his nose.

DR. JACK TEPPER, Chattanooga, Tenn.: Let us assume that an 8 year old child whose adenoids have been removed has nasal polyps. Should the polyps be removed, or should allergic studies be made first? What about the use of diphenhydramine hydrochloride ("benadryl hydrochloride") in these cases?

DR. S. A. FRIEDBERG, Chicago: If possible, the allergic studies should be made immediately. Everyone has noted regression in the size of nasal polyps in persons whose allergy has been controlled. It may be necessary to remove the large polyps before this result can be achieved. The relief afforded by diphenhydramine hydrochloride is, of course, symptomatic. I prefer to reserve the use of this drug for the severer episodes. I think it should be withheld during the period of cutaneous testing, lest the local tissue reactions be altered.

DR. J. C. JAUDON, St. Louis: Do you do a routine tonsillectomy if only adenoidectomy is necessary? If tonsillectomy is done when there is no indication for it, will there be more complications?

DR. S. A. FRIEDBERG, Chicago: No. Adenoidectomy alone is often a valuable procedure. I believe that the general tendency is toward conservatism with regard to routine tonsillectomy and adenoidectomy. There are definite surgical indications for the operation and excellent benefits to be obtained when these are followed. It is my impression (although I have no quantitative figures to support this idea) that indiscriminately performed tonsillectomies may be followed by compensatory hyperplasia of pharyngeal lymphoid tissue and that the resulting type of pharyngitis causes more distress than the previously asymptomatic tonsils.

DR. S. L. HARRISON, St. Louis: What are the indications for myringotomy?

DR. S. A. FRIEDBERG, Chicago: A combination of persistent pain, elevated temperature and a reddened, bulging tympanic membrane presents the commonest indication for myringotomy. In fact, the presence of any two of these three symptoms or signs usually warrants the procedure. I think pediatricians are becoming too reluctant to do a paracentesis. One certainly would not hesitate to incise an abscess of the finger. A tympanic cavity filled with pus presents the same problem.

DR. G. R. CLAMMER, Reading, Pa.: Is the response poorer now in cases of myringotomy because of the use of sulfonamide drugs?

DR. S. A. FRIEDBERG, Chicago: No. The combination of timely myringotomy and the proper use of sulfonamide drugs in the treatment of acute suppurative otitis media far surpasses the efficiency of either of these measures employed individually.

DR. W. E. VAN ORDER, Chattanooga, Tenn.: Does the particular type of bacteria indicate the need of paracentesis?

DR. S. A. FRIEDBERG, Chicago: If one suspects the presence of pus in the middle ear, paracentesis should be performed. It is difficult to make cultures in all the cases of discharging ears seen in the home. All hospitalized patients with infections of the ear should have cultures made.

DR. E. A. LOEB, Fontana, Calif.: What is the treatment for early otitis media?

DR. S. A. FRIEDBERG, Chicago: Local treatment, directed to the nasal passages, nasopharynx and ears, should be instituted. If the symptoms progress, a paracentesis should be performed with or without chemotherapy or biotherapy.

DR. J E. BORDLEY, Baltimore: Mastoiditis is usually severer when chemotherapy alone has been depended on. There are more complications.

DR. E. M. BURNS, Portland, Ore.: Do you advocate adenoidectomy if there are frequent nasal infections with otitis media?

DR. J. E. BORDLEY, Baltimore: Yes. Adenoidectomy may be done despite persistent infection. One is justified in prophylactic use of sulfonamide drugs before and for five days after adenoidectomy. My colleagues and I have experienced no bad results.

DR. C. C. STEWART JR., Hanover, N. H.: Should streptomycin be used in treatment of certain specific infections?

DR. J. E. BORDLEY, Baltimore: If the patient is sick enough. We do not use it as freely as we use penicillin. The longer the drug is given, the greater the danger. Of the last 50 patients treated with streptomycin in Johns Hopkins Hospital, persistent labyrinthitis developed in 7. Thus far none of the patients has recovered normal labyrinthine function.

DR. S. A. FRIEDBERG, Chicago: It is now recognized that when streptomycin is given in large doses 80 per cent of patients will present vestibular symptoms after receiving the drug longer than three weeks. Of this group, 10 per cent may have some loss of auditory function as well.

DR. W. S. ANDERSON, Washington, D. C.: Is the use of roentgen radiation or radon before and after surgical removal of tonsils and adenoids of help?

DR. J. E. BORDLEY, Baltimore: Remove the lymphoid tissue first, then inactivate the area with radon to inhibit regrowth.

DR. R. R. O'TOOLE, Pittsburgh: How important is syringing of the ear?

DR. S. A. FRIEDBERG, Chicago: The first objective in acute otitis media is to maintain established drainage. Spot suction is good. Keeping the canal wiped out to prevent caking and crusting of secretion is valuable. I have never been convinced that there is any medicational value in syringing the ear. There is some danger in the hands of an inexperienced attendant.

DR. J. E. BORDLEY, Baltimore: We have abandoned the "wet" treatment. Spot suction may be used if needed. In general, the less ear drops are used, the better.

DR. J. K. MACK, Springfield, Ill.: How young a child may be examined with the nasopharyngoscope?

DR. J. E. BORDLEY, Baltimore: We have used a child-sized nasopharyngoscope with a 3½ month old child. The procedure is not difficult. The most difficult age is 8 years. Anesthesia is usually necessary.

DR. J. S. HUNT, Charlotte, N. C.: What is the pediatrician's indication for paracentesis of the ear drum?

DR. S. A. FRIEDBERG, Chicago: A reddened, bulging drum associated with either fever or pain.

Book Reviews

Bone and Bones: Fundamentals of Bone Biology. By Joseph P. Weimann, M.D., and Harry Sicher, M.D. Price, $10. Pp. 423. St. Louis: The C. V. Mosby Company, 1947.

With the exception of the volume dealing with bone tumors by Geschickter and Copeland, texts which describe in adequate detail the structure, growth, physiology and pathology of bone have not appeared in the English literature. This is a volume which has been needed for a long time and should be welcomed by all men who have a true scientific interest in orthopedic problems.

One of the authors of this book is a pathologist and the other an anatomist, and the result of combining their knowledge in one volume has proved to be a very happy one.

The studies which have made this book possible were carried out in the Department of Research at Loyola University School of Dentistry, an institution from which other notable texts and research studies have come in years past. The section on pathology of bones is exceptionally inclusive and thorough, dealing with developmental disturbances, adaptational deformities, the influence of endocrine glands, vitamins and the effect of minerals on the bones.

The photomicrographs are noteworthy from the standpoint of careful selection and clarity of detail. In the chapter headed "Necrosis of Bone and Inflammation of Bones" the discussion of aseptic necrosis is exceptionally timely and accurate. Tumors of the skeleton are covered rather briefly, but again the quality of the photomicrographs with a magnification of 1300 makes this chapter one of the most useful in the book.

This is a book which should be in the library of every orthopedic surgeon, dentist, orthodontist, radiologist and pathologist who has a real interest in obtaining better understanding of clinical or research problems of bone and bones.

Experiences with Folic Acid. Tom D. Spies, M.D. Price, $3.75. Pp. 101. Chicago: Year Book Publishers, Inc., 1947.

From the title alone and the well earned reputation of the author, the average physician might expect that here is the discussion he has been waiting for and has sorely needed—a final summation of the value of folic acid, the new and dramatic antianemic preparation that has been so well ballyhoo'd by detail men, written up in usual extravagant and inaccurate fashion by deKruif, and popularized in medical as well as in lay publications. Unfortunately, the present small volume fails to clear up several important questions.

Dr. Spies's attitude toward folic acid seems to lack objectivity. There is a bit too much of the missionary spirit of pushing on others one's own faith in a new mode of treatment. Some case reports suggest such dramatic and prompt response to folic acid as to smack of everyday testimonials for a patent medicine. These cases are insufficiently documented by details of clinical and laboratory observations. In contrast, the discussion of the chemistry and properties of folic acid are too detailed for the average physician. More important, very little proof is offered here that folic acid is as good as liver or liver extract for the treatment of addisonian

pernicious anemia, megaloblastic anemia or sprue. In fact, evidence which has been accumulating in the past four months suggests that folic acid cannot be given in place of liver extract to patients with primary anemia, since the response of the blood in some cases is neither as good nor are the neurologic symptoms prevented or controlled by this therapy. In addition, everyone who has tried folic acid for a patient with macrocytic anemia quickly realizes that the need for daily therapy, either orally or parenterally, is a great nuisance compared to the weekly, biweekly or even monthly use of liver extract, which works so efficiently in such patients.

Possibly folic acid will sometimes prove helpful either alone or in conjunction with other medications, in the treatment of some of the rare types of anemia, or may even be a valuable agent, in its simple or conjugated form, for the treatment of conditions other than anemia. Certainly much more work, experience and objective review of the results of treatment with folic acid are necessary before its usefulness, limitations and proper place in medicine can be fully described, as is prematurely attempted in this book.

Nuevas orientaciones en la dietética del lactante. José Raúl Vásquez. Paper. Pp. 125. Buenos Aires, 1946.

This volume discusses the theory and application of Bessau's ideas in the feeding of infants. The author states that the stools of the breast-fed infant contain a uniform and regular flora represented by the bacillus Bifidus communis. Bessau in 1938 outlined a cow's milk mixture which when fed to an infant would favor the growth of such organisms. This consisted of cow's milk, acidified and predigested, with added corn starch, lactose, cystine, sesame oil, egg yolk and ascorbic acid. Later this was modified by changing the dilution, using rice instead of corn starch, splitting polysaccharide with diastase and omitting the predigestion and the sesame oil and egg yolk. He used this for healthy babies, premature infants, for patients with celiac diseases and others.

Infants given these formulas were well nourished, gained well, developed normally and had immunity similar to a breast-fed infant. The second (modified) formula proved more effective than the first. It did not prevent rickets or seborrheic dermatitis nor improve eczema. It favored the development in the feces of a gram-positive flora, was capable of maintaining an already established "bifidus" flora, and transforming a mixed or gram-negative to a gram-positive flora.

The various chemical constituents of the diet are considered in detail as well as the intestinal flora. Summaries of 70 cases are reported and there is an extensive bibliography.

Muscle Testing. By Louise Daniels, Marian Williams and Catherine Worthingham. Pp. 189. Philadelphia: W. B. Saunders Company, 1946.

This loose-leaf manual is intended for the instruction of physical therapeutists in manual muscle examination and for the reference of physical therapeutists in their practical work with patients. The system described is essentially the Lovett System, the ability of the muscle to overcome gravity and resistance being used as the objective measure of strength. The examination technic of individual muscles is described briefly and illustrated with many line drawings taken from photographs. This is an excellent manual for the novice to use for reference during manual examination of muscles. It should also be extremely useful in the classroom for teaching students of physical therapy to make such examinations. The brief description of the prime movers of individual motion with their origins and insertions,

and the accessory muscles involved, should be of material assistance in teaching muscle function to students. The anatomic drawings are largely of the muscles of the upper and lower extremities and innervation charts previously published by the Stanford University Press.

This manual can be recommended as an excellent, practical, standardized recapitulation of standard methods of testing muscles. It should be of great value to those interested in the study of muscle function and in the evaluation of muscle strength. This includes some physicians, especially those in the field of physical medicine, as well as physical therapy.

The Challenge of Polio. Roland H. Berg. Price, $2.50. Pp. 202. New York: The Dial Press, 1946.

The author has ably condensed the history of, and the research trends in, poliomyelitis, with surprisingly little distortion or bias. The material is presented in such a manner that the book is exceptionally readable, and should be easily comprehended by the nonprofessional reader, for whom it appears to be primarily intended. One is constantly aware that the author has an extraordinary knowledge of his subject, together with obvious ability as a medical reporter.

Essentials of Endocrinology. Second edition. By Arthur Grollman, M.D. Price, $10. Pp. 115. Philadelphia: J. B. Lippincott Company, 1947.

This is the second edition of a volume first published in 1941. In the preface the author says, "Clinical endocrinology is frequently befuddled by accepting unproved assumptions as basic facts and building upon the insecure foundations thus established a maze of fanciful and ill-founded conjectures. When reduced to its experimentally established facts clinical endocrinology can be placed on a scientifically sound basis." This aim has been fully realized in this book, for the author has been ruthless in discarding time honored ideas when recent advances in endocrinology failed to support them. Despite the fascination of the more imaginative phases of the text on clinical endocrinology of an earlier period, these have been gradually abandoned as experimentally established facts revealed their inaccuracy.

The discussions of physiology which are presented gland by gland before the clinical aspect is outlined are particularly valuable. The selection of the essential facts from the tremendous amount of material which has been amassed in recent years of intensive laboratory investigation has been skilfully done. Through their organization and clarity of style these discussions are eminently readable, and through omission of irrelevant material, less confusing than many other similar ones.

The book is divided into sections on Endocrine Glands of the Cranial Cavity, Bronchiogenic Organs (an advance advertisement from the publishers stating that a section on "Bronchiogenic Organs" was included had left the reviewer in a state of considerable puzzlement), Endocrine Organs of the Abdominal Cavity, Hormones of the Reproductive System, and Hormones Derived from Non-endocrine Organs. One chapter is devoted to The Hypothalamus which, though it is part of the central nervous system and not an endocrine gland, is so closely associated with endocrine organs and so vitally concerned in many metabolic and reproductive functions as to warrant its inclusion.

References are well selected with emphasis on recent monographs, which enable the reader to seek further and more detailed information where desired.

This is a most welcome addition to the small group of books which the practitioner keeps on his desk, rather than on the shelf.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Pan American Congress of Pediatrics

President: Dr. Felix Hurtado, Habana, Cuba.

Save the Children International Union

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quai Wilson, Geneva, Switzerland.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secçaõ de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff, Hospital for Sick Children, Great Ormond St, London, W. 1.

Danish Pediatric Society

President: Prof. E. Lenstrup, Copenhagen.
Secretary: Dr. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. L. Keyzer, 114 St. Josephstr., Tilburg.
Secretary: Dr. H. Reerink, 2B Paul Krugerstr., Arnheim.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASES IN CHILDREN

President: Dr. W. G. Wyllie, 33 Wimpole St., London W. 1, England.
Secretary: Dr. Philip Rainsford Evans, Keat's House, Guy's Hospital, London S. E. 1, England.
Place: 1 Wimpole St., London W. 1. Time: Fourth Friday of each month, 4:15 p. m.

SOCIEDAD BOLIVIANA DE PEDIATRIA

President: Dr. Ernesto Trigo Pizarro.
Secretary: Dr. Carlos Ferrufino, Casilla 272, La Paz, Bolivia.
Place: La Paz, Bolivia.

SOCIEDAD CHILENA DE PEDIATRIA

President: Mr. Cesar Izzo Parodi, Merced 565, Santiago, Chile.
General Secretary: Dr. Jorge Peña Cereceda, Santiago, Chile.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Teodosio Valledor, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedes y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

SOCIEDAD DOMINICANA DE PEDIATRIA

President: Dr. Alberto Peguero, Ciudad Trujillo, R.D.
Secretary-Treasurer: Dr. Jaime Jorge, Ciudad Trujillo, R.D.
Place: Children's Ramfis Hospital. Time: 8 p. m., last Thursday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Antonio Prado Vértiz, Edison 101, Mexico City, Mexico.
Secretary: Dr. Manuel Mendez, Hospital del Niño Mexico City, Mexico.

SOCIEDAD DE PEDIATRÍA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 2000, Esq. Ocaña (N.), Córdoba, Argentina.
Place: Comite pro Defenso del Niño, Dean Funes 2000, Córdoba, Argentina. Time: Once a month.

SOCIEDAD DE PEDIATRIA DEL LITORAL

President: Dr. Jose E. Celoria, Hospital Centenario, Rosario, Argentina.
Secretary: Dr. Gloria Lovell, Hospital Centenario, Rosario, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

Sociedad Venezolana de Puericultura y Pediatria

President: Dr. Pastor Oropeza, Caracas.
Secretary: Dr. Carlos E. Castillo, Hospital Municipal de Niños, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

Société de Pédiatrie de Paris

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

Swedish Medical Society, Section for Pediatrics and School Hygiene

President: Prof. Arvid Wallgren, 53 Strandvägen, Stockholm.
Secretary: Dr. Henning Magnusson, 58 Odengatan, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

Uruguayan Society of Pediatrics

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenda Agraciado 1464 (Piso 13), Montevideo.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Oscar Reiss, 2200 W. 3d St., Los Angeles.
Secretary: Dr. Margaret Mary Nicholson, 1801 Eye St. N. W., Washington, D. C.
Place: Chicago. Time: June 21-25, 1948.

American Academy of Pediatrics

President: Dr. Jay I. Durand, 515 Cobb Bldg., Seattle, Wash.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Atlantic City, N. J. Time: Nov. 20-23, 1948.
Regional Meetings:
Place: Milwaukee, Wis. Time: June 28-30, 1948.
Place: Seattle, Wash. Time: Sept. 13-15, 1948.

American Hospital Association, Massachusetts Hospital Association

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.

American Pediatric Society

President: Dr. Harold K. Faber, 2361 Clay St., San Francisco.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

Canadian Society for the Study of diseases of Children

President:: Dr. Alan Ross, 1414 Drummond St., Montreal.
Secretary-Treasurer: Dr. R. L. Denton, 3534 Ontario Ave., Montreal.

Society for Pediatric Research

President: Dr. Donovan J. McCune, 3975 Broadway, New York.
Secretary: Dr. Robert Ward, Bellevue Hospital, New York 16.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Wesley H. Anderson, 2404 Washington Blvd., Ogden, Utah.
Secretary-Treasurer: Dr. F. M. Kriete, State Capitol, Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Secretary-Treasurer: Dr. Charles D. May, 300 Longwood Ave., Boston
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Percy Guy, 502–2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. George Kimmel, Redwing, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Jackson L. Sadler, 109 W. Olive St., Ft. Collins, Colo.
Secretary: Dr. Edwin T. Williams, 1850 Gilpin St., Denver 6.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. Stewart H. Welch, 117 S. 20th St., Birmingham 5, Ala.
Secretary: Dr. W. Ambrose McGee, 1601 Monument Ave., Richmond 20, Va.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Ruth Berrey, 2211 Highland Ave., Birmingham 5, Ala.
Secretary-Treasurer: Dr. W. A. Daniel Jr., 115 S. Union St., Montgomery 5, Ala.
Place: Birmingham. Time: September 1948.

ARIZONA PEDIATRIC SOCIETY

President: Dr. W. P. Sherrill, 342 W. McDowell Rd., Phoenix.
Secretary: Dr. W. F. Schoffman, 926 E. McDowell Rd., Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truston Ave., Bakersfield.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. James R. Boulware, Lakeland.
Secretary: Dr. Hugh A. Carithers, 2000 Park St., Jacksonville 4.
Place: Concurrent with state association convention and fall meeting.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. F. M. Meyer, 144 Golden Hill St., Bridgeport, Conn.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Frederick H. Maurer, 331 Fulton St., Peoria 2.
Secretary: Dr. Eugene T. McEnery, 4458 W. Madison St., Chicago.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolic.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.
Secretary-Treasurer: Dr. James Dunn, 414 Blackhawk Hotel, Davenport.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. R. V. Platou, 1430 Tulane Ave., New Orleans 13.
Secretary-Treasurer: Dr. Bertha Wexler, 3439 Prytania St., New Orleans 15.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Joseph A. Gilmartin, 3700–5th Ave., Pittsburgh 13.
Secretary: Dr. Carl C. Fischer, 100 W. Coulter St., Philadelphia 44.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. J. H. Lewis, 2956 Biddle Ave., Wyandotte.
Secretary: Dr. Robert H. Trimby, 122 W. Hillsdale, Lansing.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. Paul N. Marrow, 1614 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Michael Crofoot, 1407 Medical Arts Bldg., Omaha 2.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW MEXICO STATE PEDIATRIC SOCIETY

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Charles R. Bugg, Professional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. J. B. Snow, 625 N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston.

TENNESSEE PEDIATRIC SOCIETY

President: Dr. Harold J. Starr, 803 Medical Arts Bldg., Chattanooga 3.
Secretary-Treasurer: Dr. W. O. Vaughan, 2105 Hayes St., Nashville 5.
Time: Second Monday in April.

TEXAS PEDIATRC SOCIETY

President: Dr. Charles B. Alexander, 1716 Nix Professional Bldg., San Antonio 5.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.
Secretary: Dr. Louise Galvin, 214 S. Boulevard, Richmond 21.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.

WISCONSIN STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. M. G. Peterman, 411 E. Mason St., Milwaukee 2.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

BALTIMORE CITY MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Charles O'Donovan Jr., 5 E. Read St., Baltimore.
Secretary: Dr. T. Campbell Goodwin, 16 E. Biddle St., Baltimore.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry S. Pizer, 1726 Davidson Ave., New York.
Secretary: Dr. Nathan M. Greenstein, 1488 Metropolitan Ave., New York.
Place: Morrisania City Hospital. Time: 8:30 p. m., second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. George E. Brockway Jr., 176 Fenimore St., Brooklyn.
Secretary: Dr. Bernard Benjamin, 845 Park Pl., Brooklyn 16.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, October and November.

BUFFALO PEDIATRIC SOCIETY

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. H. William Elghammer, 2371 E. 71st St., Chicago.
Secretary: Dr. Alvah L. Newcomb, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Leo S. Friedman, 666 Rockdale Ave., Cincinnati 29.
Secretary: Dr. George Renner, 3144 Jefferson Ave., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. Shirley Hodges, 2703 Oak Lawn Ave., Dallas, Texas.
Secretary-Treasurer: Frances M. Love, 4585 Belfort, Dallas 4.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m., the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Otto Grob, 651 Fisher Bldg., Detroit 2, Mich.
Secretary: Dr. Harold B. Rothbart, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Third Wednesday of each month.

Houston Pediatric Society

President: Dr. George Salmon, 1220 Bartlett St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., last Tuesday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Knoxville–Oak Ridge Pediatric Society

President: Dr. Henry S. Christian, 205 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. John Eggleston, Oak Ridge Hospital, Oak Ridge, Tenn.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles 26.
Secretary-Treasurer: Dr. Robert Simonds, 267 S. Beverly Dr., Beverly Hills, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Samuel K. Levy, 1694 Nostrand Ave., Brooklyn 26.
Secretary: Dr. Samuel Silber, 865 Park Pl., Brooklyn 16.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02–91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Louis Appel, 143-42 Cherry Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION ON PEDIATRICS

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. M. G. Peterman, 411 E. Mason St., Milwaukee 2, Wis.
Secretary-Treasurer: Dr. Katharine Baird, 1411 Wauwatosa Ave., Wauwatosa 13, Wis.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman Dr. Robert O. Du Bois, 122 E. 76th St., New York.
Secretary: Dr. Harold W. Dargeon, 1095 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

OKLAHOMA CITY PEDIATRIC SOCIETY

President: Dr. J. B. Snow, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Arthur M. Dannenburg, 235 S. 15th St., Philadelphia 2.
Secretary: Dr. D. Stewart Polk, Rosemont, Pa.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday from October to May, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Jerome Glaser, 300 S. Goodman St., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Daniel B. Peeler, 1162 Lake Ave., Rochester 13, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.
Time: Second Thursday of each month from October to May, inclusive.

San Antonio Pediatric Society

President: Dr. Sidney R. Kaliski, 518 Moore Bldg., San Antonio 5.
Secretary-Treasurer: Dr. Edith M. Bonnet, 228 Medical Arts Bldg., San Antonio 5.
Place: Variable. Time: 7:30 p. m., first Tuesday of every month.

Seattle Pediatric Society

President: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle 1.
Secretary: Dr. Jack M. Doctor, 738 Broadway, Seattle 22.
Place: College Club. Time: Fourth Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Donald C. Shelby, 416 N. Bedford Dr., Beverly Hills, Calif.
Secretary: Dr. Harry F. Dietrich, 416 N. Bedford Dr., Beverly Hills, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.